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(54) Title: NOVEL NUCLEIC ACIDS AND POLYPEPTIDES

(57) Abstract: The present invention provides novel nucleic acids, polypeptide sequences encoded by these nucleic acids and uses thereof.

NOVEL NUCLEIC ACIDS AND POLYPEPTIDES

1. TECHNICAL FIELD

The present invention provides novel polynucleotides and proteins encoded by such polynucleotides, along with uses for these polynucleotides and proteins, for example in therapeutic, diagnostic and research methods.

2. BACKGROUND

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Technology aimed at the discovery of protein factors (including e.g., cytokines, such as lymphokines, interferons, circulating soluble factors, chemokines, and interleukins) has matured rapidly over the past decade. The now routine hybridization cloning and expression cloning techniques clone novel polynucleotides "directly" in the sense that they rely on information directly related to the discovered protein (i.e., partial DNA/amino acid sequence of the protein in the case of hybridization cloning; activity of the protein in the case of expression cloning). More recent "indirect" cloning techniques such as signal sequence cloning, which isolates DNA sequences based on the presence of a now well-recognized secretory leader sequence motif, as well as various PCR-based or low stringency hybridization-based cloning techniques, have advanced the state of the art by making available large numbers of DNA/amino acid sequences for proteins that are known to have biological activity, for example, by virtue of their secreted nature in the case of leader sequence cloning, by virtue of their cell or tissue source in the case of PCR-based techniques, or by virtue of structural similarity to other genes of known biological activity.

Identified polynucleotide and polypeptide sequences have numerous applications in, for example, diagnostics, forensics, gene mapping; identification of mutations responsible for genetic disorders or other traits, to assess biodiversity, and to produce many other types of data and products dependent on DNA and amino acid sequences.

3. SUMMARY OF THE INVENTION

The compositions of the present invention include novel isolated polypeptides, novel isolated polynucleotides encoding such polypeptides, including recombinant DNA molecules, cloned genes or degenerate variants thereof, especially naturally occurring variants such as allelic variants, antisense polynucleotide molecules, and antibodies that specifically recognize

one or more epitopes present on such polypeptides, as well as hybridomas producing such antibodies.

The compositions of the present invention additionally include vectors, including expression vectors, containing the polynucleotides of the invention, cells genetically engineered to contain such polynucleotides and cells genetically engineered to express such polynucleotides.

The present invention relates to a collection or library of at least one novel nucleic acid sequence assembled from expressed sequence tags (ESTs) isolated mainly by sequencing by hybridization (SBH), and in some cases, sequences obtained from one or more public databases. The invention relates also to the proteins encoded by such polynucleotides, along with therapeutic, diagnostic and research utilities for these polynucleotides and proteins. These nucleic acid sequences are designated as SEQ ID NO: 1-93. The polypeptides sequences are designated SEQ ID NO: 94-186. The nucleic acids and polypeptides are provided in the Sequence Listing. In the nucleic acids provided in the Sequence Listing, A is adenosine; C is cytosine; G is guanine; T is thymine; and N is unknown or any of the four bases.

The nucleic acid sequences of the present invention also include, nucleic acid sequences that hybridize to the complement of SEQ ID NO: 1-93 under stringent hybridization conditions; nucleic acid sequences which are allelic variants or species homologues of any of the nucleic acid sequences recited above, or nucleic acid sequences that encode a peptide comprising a specific domain or truncation of the peptides encoded by SEQ ID NO: 1-93. A polynucleotide comprising a nucleotide sequence having at least 90% identity to an identifying sequence of SEQ ID NO: 1-93 or a degenerate variant or fragment thereof. The identifying sequence can be 100 base pairs in length.

The nucleic acid sequences of the present invention also include the sequence information from the nucleic acid sequences of SEQ ID NO: 1-93. The sequence information can be a segment of any one of SEQ ID NO: 1-93 that uniquely identifies or represents the sequence information of SEQ ID NO: 1-93.

A collection as used in this application can be a collection of only one polynucleotide. The collection of sequence information or identifying information of each sequence can be provided on a nucleic acid array. In one embodiment, segments of sequence information are provided on a nucleic acid array to detect the polynucleotide that contains the segment. The array can be designed to detect full-match or mismatch to the polynucleotide that contains the segment. The collection can also be provided in a computer-readable format.

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This invention also includes the reverse or direct complement of any of the nucleic acid sequences recited above; cloning or expression vectors containing the nucleic acid sequences; and host cells or organisms transformed with these expression vectors. Nucleic acid sequences (or their reverse or direct complements) according to the invention have numerous applications in a variety of techniques known to those skilled in the art of molecular biology, such as use as hybridization probes, use as primers for PCR, use in an array, use in computer-readable media, use in sequencing full-length genes, use for chromosome and gene mapping, use in the recombinant production of protein, and use in the generation of anti-sense DNA or RNA, their chemical analogs and the like.

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In a preferred embodiment, the nucleic acid sequences of SEQ ID NO: 1-93 or novel segments or parts of the nucleic acids of the invention are used as primers in expression assays that are well known in the art. In a particularly preferred embodiment, the nucleic acid sequences of SEQ ID NO: 1-93 or novel segments or parts of the nucleic acids provided herein are used in diagnostics for identifying expressed genes or, as well known in the art and exemplified by Vollrath et al., Science 258:52-59 (1992), as expressed sequence tags for physical mapping of the human genome.

The isolated polynucleotides of the invention include, but are not limited to, a polynucleotide comprising any one of the nucleotide sequences set forth in SEQ ID NO: 1-93; a polynucleotide comprising any of the full length protein coding sequences of SEQ ID NO: 1-93; and a polynucleotide comprising any of the nucleotide sequences of the mature protein coding sequences of SEQ ID NO: 1-93. The polynucleotides of the present invention also include, but are not limited to, a polynucleotide that hybridizes under stringent hybridization conditions to (a) the complement of any one of the nucleotide sequences set forth in SEQ ID NO: 1-93; (b) a nucleotide sequence encoding any one of the amino acid sequences set forth in the Sequence Listing; (c) a polynucleotide which is an allelic variant of any polynucleotides recited above; (d) a polynucleotide which encodes a species homolog (e.g. orthologs) of any of the proteins recited above; or (e) a polynucleotide that encodes a polypeptide comprising a specific domain or truncation of any of the polypeptides comprising an amino acid sequence set forth in the Sequence Listing.

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The isolated polypeptides of the invention include, but are not limited to, a polypeptide comprising any of the amino acid sequences set forth in SEQ ID NO: 94-186; or the corresponding full length or mature protein. Polypeptides of the invention also include polypeptides with biological activity that are encoded by (a) any of the polynucleotides having a

nucleotide sequence set forth in SEQ ID NO: 1-93; or (b) polynucleotides that hybridize to the complement of the polynucleotides of (a) under stringent hybridization conditions. Biologically or immunologically active variants of any of the polypeptide sequences in the Sequence Listing, and "substantial equivalents" thereof (e.g., with at least about 65%, 70%, 75%, 80%, 85%, 90%, 95%, 98% or 99% amino acid sequence identity) that preferably retain biological activity are also contemplated. The polypeptides of the invention may be wholly or partially chemically synthesized but are preferably produced by recombinant means using the genetically engineered cells (e.g. host cells) of the invention.

The invention also provides compositions comprising a polypeptide of the invention. Polypeptide compositions of the invention may further comprise an acceptable carrier, such as a hydrophilic, e.g., pharmaceutically acceptable, carrier.

The invention also provides host cells transformed or transfected with a polynucleotide of the invention.

The invention also relates to methods for producing a polypeptide of the invention comprising growing a culture of the host cells of the invention in a suitable culture medium under conditions permitting expression of the desired polypeptide, and purifying the polypeptide from the culture or from the host cells. Preferred embodiments include those in which the protein produced by such process is a mature form of the protein.

Polynucleotides according to the invention have numerous applications in a variety of techniques known to those skilled in the art of molecular biology. These techniques include use as hybridization probes, use as oligomers, or primers, for PCR, use for chromosome and gene mapping, use in the recombinant production of protein, and use in generation of anti-sense DNA or RNA, their chemical analogs and the like. For example, when the expression of an mRNA is largely restricted to a particular cell or tissue type, polynucleotides of the invention can be used as hybridization probes to detect the presence of the particular cell or tissue mRNA in a sample using, e.g., in situ hybridization.

In other exemplary embodiments, the polynucleotides are used in diagnostics as expressed sequence tags for identifying expressed genes or, as well known in the art and exemplified by Vollrath et al., Science 258:52-59 (1992), as expressed sequence tags for physical mapping of the human genome.

The polypeptides according to the invention can be used in a variety of conventional procedures and methods that are currently applied to other proteins. For example, a polypeptide of the invention can be used to generate an antibody that specifically binds the

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polypeptide. Such antibodies, particularly monoclonal antibodies, are useful for detecting or quantitating the polypeptide in tissue. The polypeptides of the invention can also be used as molecular weight markers, and as a food supplement.

Methods are also provided for preventing, treating, or ameliorating a medical condition which comprises the step of administering to a mammalian subject a therapeutically effective amount of a composition comprising a polypeptide of the present invention and a pharmaceutically acceptable carrier.

In particular, the polypeptides and polynucleotides of the invention can be utilized, for example, in methods for the prevention and/or treatment of disorders involving aberrant protein expression or biological activity.

The present invention further relates to methods for detecting the presence of the polynucleotides or polypeptides of the invention in a sample. Such methods can, for example, be utilized as part of prognostic and diagnostic evaluation of disorders as recited herein and for the identification of subjects exhibiting a predisposition to such conditions. The invention provides a method for detecting the polynucleotides of the invention in a sample, comprising contacting the sample with a compound that binds to and forms a complex with the polynucleotide of interest for a period sufficient to form the complex and under conditions sufficient to form a complex and detecting the complex such that if a complex is detected, the polynucleotide of interest is detected. The invention also provides a method for detecting the polypeptides of the invention in a sample comprising contacting the sample with a compound that binds to and forms a complex with the polypeptide under conditions and for a period sufficient to form the complex and detecting the formation of the complex such that if a complex is formed, the polypeptide is detected.

The invention also provides kits comprising polynucleotide probes and/or monoclonal antibodies, and optionally quantitative standards, for carrying out methods of the invention. Furthermore, the invention provides methods for evaluating the efficacy of drugs, and monitoring the progress of patients, involved in clinical trials for the treatment of disorders as recited above.

The invention also provides methods for the identification of compounds that modulate (i.e., increase or decrease) the expression or activity of the polynucleotides and/or polypeptides of the invention. Such methods can be utilized, for example, for the identification of compounds that can ameliorate symptoms of disorders as recited herein. Such methods can include, but are not limited to, assays for identifying compounds and other

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substances that interact with (e.g., bind to) the polypeptides of the invention. The invention provides a method for identifying a compound that binds to the polypeptides of the invention comprising contacting the compound with a polypeptide of the invention in a cell for a time sufficient to form a polypeptide/compound complex, wherein the complex drives expression of a reporter gene sequence in the cell; and detecting the complex by detecting the reporter gene sequence expression such that if expression of the reporter gene is detected the compound the binds to a polypeptide of the invention is identified.

The methods of the invention also provide methods for treatment which involve the administration of the polynucleotides or polypeptides of the invention to individuals exhibiting symptoms or tendencies. In addition, the invention encompasses methods for treating diseases or disorders as recited herein comprising administering compounds and other substances that modulate the overall activity of the target gene products. Compounds and other substances can effect such modulation either on the level of target gene/protein expression or target protein activity.

The polypeptides of the present invention and the polynucleotides encoding them are also useful for the same functions known to one of skill in the art as the polypeptides and polynucleotides to which they have homology (set forth in Table 2); for which they have a signature region (as set forth in Table 3); or for which they have homology to a gene family (as set forth in Table 4). If no homology is set forth for a sequence, then the polypeptides and polynucleotides of the present invention are useful for a variety of applications, as described herein, including use in arrays for detection.

4. DETAILED DESCRIPTION OF THE INVENTION

25 4.1 DEFINITIONS

It must be noted that as used herein and in the appended claims, the singular forms "a", "an" and "the" include plural references unless the context clearly dictates otherwise.

The term "active" refers to those forms of the polypeptide which retain the biologic and/or immunologic activities of any naturally occurring polypeptide. According to the invention, the terms "biologically active" or "biological activity" refer to a protein or peptide having structural, regulatory or biochemical functions of a naturally occurring molecule. Likewise "immunologically active" or "immunological activity" refers to the capability of the

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natural, recombinant or synthetic polypeptide to induce a specific immune response in appropriate animals or cells and to bind with specific antibodies.

The term "activated cells" as used in this application are those cells which are engaged in extracellular or intracellular membrane trafficking, including the export of secretory or enzymatic molecules as part of a normal or disease process.

The terms "complementary" or "complementarity" refer to the natural binding of polynucleotides by base pairing. For example, the sequence 5'-AGT-3' binds to the complementary sequence 3'-TCA-5'. Complementarity between two single-stranded molecules may be "partial" such that only some of the nucleic acids bind or it may be "complete" such that total complementarity exists between the single stranded molecules. The degree of complementarity between the nucleic acid strands has significant effects on the efficiency and strength of the hybridization between the nucleic acid strands.

The term "embryonic stem cells (ES)" refers to a cell that can give rise to many differentiated cell types in an embryo or an adult, including the germ cells. The term "germ line stem cells (GSCs)" refers to stem cells derived from primordial stem cells that provide a steady and continuous source of germ cells for the production of gametes. The term "primordial germ cells (PGCs)" refers to a small population of cells set aside from other cell lineages particularly from the yolk sac, mesenteries, or gonadal ridges during embryogenesis that have the potential to differentiate into germ cells and other cells. PGCs are the source from which GSCs and ES cells are derived. The PGCs, the GSCs and the ES cells are capable of self-renewal. Thus these cells not only populate the germ line and give rise to a plurality of terminally differentiated cells that comprise the adult specialized organs, but are able to regenerate themselves.

The term "expression modulating fragment," EMF, means a series of nucleotides which modulates the expression of an operably linked ORF or another EMF.

As used herein, a sequence is said to "modulate the expression of an operably linked sequence" when the expression of the sequence is altered by the presence of the EMF. EMFs include, but are not limited to, promoters, and promoter modulating sequences (inducible elements). One class of EMFs are nucleic acid fragments which induce the expression of an operably linked ORF in response to a specific regulatory factor or physiological event.

The terms "nucleotide sequence" or "nucleic acid" or "polynucleotide" or "oligonculeotide" are used interchangeably and refer to a heteropolymer of nucleotides or the sequence of these nucleotides. These phrases also refer to DNA or RNA of genomic or

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synthetic origin which may be single-stranded or double-stranded and may represent the sense or the antisense strand, to peptide nucleic acid (PNA) or to any DNA-like or RNA-like material. In the sequences herein A is adenine, C is cytosine, T is thymine, G is guanine and N is A, C, G or T (U). It is contemplated that where the polynucleotide is RNA, the T (thymine) in the sequences provided herein is substituted with U (uracil). Generally, nucleic acid segments provided by this invention may be assembled from fragments of the genome and short oligonucleotide linkers, or from a series of oligonucleotides, or from individual nucleotides, to provide a synthetic nucleic acid which is capable of being expressed in a recombinant transcriptional unit comprising regulatory elements derived from a microbial or viral operon, or a eukaryotic gene.

The terms "oligonucleotide fragment" or a "polynucleotide fragment", "portion," or "segment" or "probe" or "primer" are used interchangeably and refer to a sequence of nucleotide residues which are at least about 5 nucleotides, more preferably at least about 7 nucleotides, more preferably at least about 11 nucleotides, more preferably at least about 11 nucleotides and most preferably at least about 17 nucleotides. The fragment is preferably less than about 500 nucleotides, preferably less than about 200 nucleotides, more preferably less than about 100 nucleotides, more preferably less than about 50 nucleotides and most preferably less than 30 nucleotides. Preferably the probe is from about 6 nucleotides to about 200 nucleotides, preferably from about 15 to about 50 nucleotides, more preferably from about 17 to 30 nucleotides and most preferably from about 20 to 25 nucleotides. Preferably the fragments can be used in polymerase chain reaction (PCR), various hybridization procedures, or microarray procedures to identify or amplify identical or related parts of mRNA or DNA molecules. A fragment or segment may uniquely identify each polynucleotide sequence of the present invention. Preferably the fragment comprises a sequence substantially similar to any one of SEO ID NO: 1-93.

Probes may, for example, be used to determine whether specific mRNA molecules are present in a cell or tissue or to isolate similar nucleic acid sequences from chromosomal DNA as described by Walsh et al. (Walsh, P.S. et al., 1992, PCR Methods Appl 1:241-250). They may be labeled by nick translation, Klenow fill-in reaction, PCR, or other methods well known in the art. Probes of the present invention, their preparation, and/or labeling are elaborated in Sambrook, J. et al., 1989, Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Laboratory, NY; or Ausubel, F.M. et al., 1989, Current Protocols in Molecular

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Biology, John Wiley & Sons, New York NY, both of which are incorporated herein by reference in their entirety.

The nucleic acid sequences of the present invention also include the sequence information from the nucleic acid sequences of SEQ ID NO: 1-93. The sequence information can be a segment of any one of SEQ ID NO: 1-93 that uniquely identifies or represents the sequence information of that sequence of SEQ ID NO: 1-93. One such segment can be a twenty-mer nucleic acid sequence because the probability that a twenty-mer is fully matched in the human genome is 1 in 300. In the human genome, there are three billion base pairs in one set of chromosomes. Because 4²⁰ possible twenty-mers exist, there are 300 times more twenty-mers than there are base pairs in a set of human chromosomes. Using the same analysis, the probability for a seventeen-mer to be fully matched in the human genome is approximately 1 in 5. When these segments are used in arrays for expression studies, fifteenmer segments can be used. The probability that the fifteen-mer is fully matched in the expressed sequences is also approximately one in five because expressed sequences comprise less than approximately 5% of the entire genome sequence.

Similarly, when using sequence information for detecting a single mismatch, a segment can be a twenty-five mer. The probability that the twenty-five mer would appear in a human genome with a single mismatch is calculated by multiplying the probability for a full match $(1\div4^{25})$ times the increased probability for mismatch at each nucleotide position (3 x 25). The probability that an eighteen mer with a single mismatch can be detected in an array for expression studies is approximately one in five. The probability that a twenty-mer with a single mismatch can be detected in a human genome is approximately one in five.

The term "open reading frame," ORF, means a series of nucleotide triplets coding for amino acids without any termination codons and is a sequence translatable into protein.

The terms "operably linked" or "operably associated" refer to functionally related nucleic acid sequences. For example, a promoter is operably associated or operably linked with a coding sequence if the promoter controls the transcription of the coding sequence. While operably linked nucleic acid sequences can be contiguous and in the same reading frame, certain genetic elements e.g. repressor genes are not contiguously linked to the coding sequence but still control transcription/translation of the coding sequence.

The term "pluripotent" refers to the capability of a cell to differentiate into a number of differentiated cell types that are present in an adult organism. A pluripotent cell is restricted in its differentiation capability in comparison to a totipotent cell.

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The terms "polypeptide" or "peptide" or "amino acid sequence" refer to an oligopeptide, peptide, polypeptide or protein sequence or fragment thereof and to naturally occurring or synthetic molecules. A polypeptide "fragment," "portion," or "segment" is a stretch of amino acid residues of at least about 5 amino acids, preferably at least about 7 amino acids, more preferably at least about 9 amino acids and most preferably at least about 17 or more amino acids. The peptide preferably is not greater than about 500 amino acids, more preferably less than 200 amino acids more preferably less than 150 amino acids, and most preferably less than 100 amino acids. Preferably the peptide is from about 5 to about 200 amino acids. To be active, any polypeptide must have sufficient length to display biological and/or immunological activity.

The term "naturally occurring polypeptide" refers to polypeptides produced by cells that have not been genetically engineered and specifically contemplates various polypeptides arising from post-translational modifications of the polypeptide including, but not limited to, acetylation, carboxylation, glycosylation, phosphorylation, lipidation and acylation.

The term "translated protein coding portion" means a sequence which encodes for the full length protein which may include any leader sequence or any processing sequence.

The term "mature protein coding sequence" means a sequence which encodes a peptide or protein without a signal or leader sequence. The "mature protein portion" means that portion of the protein which does not include a signal or leader sequence. The peptide may have been produced by processing in the cell which removes any leader/signal sequence. The mature protein portion may or may not include an initial methionine residue. The methionine residue may be removed from the protein during processing in the cell. The peptide may be produced synthetically or the protein may have been produced using a polynucleotide only encoding for the mature protein coding sequence.

The term "derivative" refers to polypeptides chemically modified by such techniques as ubiquitination, labeling (e.g., with radionuclides or various enzymes), covalent polymer attachment such as pegylation (derivatization with polyethylene glycol) and insertion or substitution by chemical synthesis of amino acids such as ornithine, which do not normally occur in human proteins.

The term "variant" (or "analog") refers to any polypeptide differing from naturally occurring polypeptides by amino acid insertions, deletions, and substitutions, created using, e g., recombinant DNA techniques. Guidance in determining which amino acid residues may be replaced, added or deleted without abolishing activities of interest, may be found by

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comparing the sequence of the particular polypeptide with that of homologous peptides and minimizing the number of amino acid sequence changes made in regions of high homology (conserved regions) or by replacing amino acids with consensus sequence.

Alternatively, recombinant variants encoding these same or similar polypeptides may be synthesized or selected by making use of the "redundancy" in the genetic code. Various codon substitutions, such as the silent changes which produce various restriction sites, may be introduced to optimize cloning into a plasmid or viral vector or expression in a particular prokaryotic or eukaryotic system. Mutations in the polynucleotide sequence may be reflected in the polypeptide or domains of other peptides added to the polypeptide to modify the properties of any part of the polypeptide, to change characteristics such as ligand-binding affinities, interchain affinities, or degradation/turnover rate.

Preferably, amino acid "substitutions" are the result of replacing one amino acid with another amino acid having similar structural and/or chemical properties, *i.e.*, conservative amino acid replacements. "Conservative" amino acid substitutions may be made on the basis of similarity in polarity, charge, solubility, hydrophobicity, hydrophilicity, and/or the amphipathic nature of the residues involved. For example, nonpolar (hydrophobic) amino acids include alanine, leucine, isoleucine, valine, proline, phenylalanine, tryptophan, and methionine; polar neutral amino acids include glycine, serine, threonine, cysteine, tyrosine, asparagine, and glutamine; positively charged (basic) amino acids include arginine, lysine, and histidine; and negatively charged (acidic) amino acids include aspartic acid and glutamic acid. "Insertions" or "deletions" are preferably in the range of about 1 to 20 amino acids, more preferably 1 to 10 amino acids. The variation allowed may be experimentally determined by systematically making insertions, deletions, or substitutions of amino acids in a polypeptide molecule using recombinant DNA techniques and assaying the resulting recombinant variants for activity.

Alternatively, where alteration of function is desired, insertions, deletions, or non-conservative alterations can be engineered to produce altered polypeptides. Such alterations can, for example, alter one or more of the biological functions or biochemical characteristics of the polypeptides of the invention. For example, such alterations may change polypeptide characteristics such as ligand-binding affinities, interchain affinities, or degradation/turnover rate. Further, such alterations can be selected so as to generate polypeptides that are better suited for expression, scale up and the like in the host cells

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chosen for expression. For example, cysteine residues can be deleted or substituted with another amino acid residue in order to eliminate disulfide bridges.

The terms "purified" or "substantially purified" as used herein denotes that the indicated nucleic acid or polypeptide is present in the substantial absence of other biological macromolecules, e.g., polynucleotides, proteins, and the like. In one embodiment, the polynucleotide or polypeptide is purified such that it constitutes at least 95% by weight, more preferably at least 99% by weight, of the indicated biological macromolecules present (but water, buffers, and other small molecules, especially molecules having a molecular weight of less than 1000 daltons, can be present).

The term "isolated" as used herein refers to a nucleic acid or polypeptide separated from at least one other component (e.g., nucleic acid or polypeptide) present with the nucleic acid or polypeptide in its natural source. In one embodiment, the nucleic acid or polypeptide is found in the presence of (if anything) only a solvent, buffer, ion, or other component normally present in a solution of the same. The terms "isolated" and "purified" do not

encompass nucleic acids or polypeptides present in their natural source.

The term "recombinant," when used herein to refer to a polypeptide or protein, means that a polypeptide or protein is derived from recombinant (e.g., microbial, insect, or mammalian) expression systems. "Microbial" refers to recombinant polypeptides or proteins made in bacterial or fungal (e.g., yeast) expression systems. As a product, "recombinant microbial" defines a polypeptide or protein essentially free of native endogenous substances and unaccompanied by associated native glycosylation. Polypeptides or proteins expressed in most bacterial cultures, e.g., E. coli, will be free of glycosylation modifications; polypeptides or proteins expressed in yeast will have a glycosylation pattern in general different from those expressed in mammalian cells.

The term "recombinant expression vehicle or vector" refers to a plasmid or phage or virus or vector, for expressing a polypeptide from a DNA (RNA) sequence. An expression vehicle can comprise a transcriptional unit comprising an assembly of (1) a genetic element or elements having a regulatory role in gene expression, for example, promoters or enhancers, (2) a structural or coding sequence which is transcribed into mRNA and translated into protein, and (3) appropriate transcription initiation and termination sequences. Structural units intended for use in yeast or eukaryotic expression systems preferably include a leader sequence enabling extracellular secretion of translated protein by a host cell. Alternatively, where recombinant protein is expressed without a leader or transport sequence, it may include

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an amino terminal methionine residue. This residue may or may not be subsequently cleaved from the expressed recombinant protein to provide a final product.

The term "recombinant expression system" means host cells which have stably integrated a recombinant transcriptional unit into chromosomal DNA or carry the recombinant transcriptional unit extrachromosomally. Recombinant expression systems as defined herein will express heterologous polypeptides or proteins upon induction of the regulatory elements linked to the DNA segment or synthetic gene to be expressed. This term also means host cells which have stably integrated a recombinant genetic element or elements having a regulatory role in gene expression, for example, promoters or enhancers. Recombinant expression systems as defined herein will express polypeptides or proteins endogenous to the cell upon induction of the regulatory elements linked to the endogenous

DNA segment or gene to be expressed. The cells can be prokaryotic or eukaryotic.

The term "secreted" includes a protein that is transported across or through a membrane, including transport as a result of signal sequences in its amino acid sequence when it is expressed in a suitable host cell. "Secreted" proteins include without limitation proteins secreted wholly (e.g., soluble proteins) or partially (e.g., receptors) from the cell in which they are expressed. "Secreted" proteins also include without limitation proteins that are transported across the membrane of the endoplasmic reticulum. "Secreted" proteins are also intended to include proteins containing non-typical signal sequences (e.g. Interleukin-1 Beta, see Krasney, P.A. and Young, P.R. (1992) Cytokine 4(2): 134 -143) and factors released from damaged cells (e.g. Interleukin-1 Receptor Antagonist, see Arend, W.P. et. al. (1998) Annu. Rev. Immunol. 16:27-55)

Where desired, an expression vector may be designed to contain a "signal or leader sequence" which will direct the polypeptide through the membrane of a cell.. Such a sequence may be naturally present on the polypeptides of the present invention or provided from heterologous protein sources by recombinant DNA techniques.

The term "stringent" is used to refer to conditions that are commonly understood in the art as stringent. Stringent conditions can include highly stringent conditions (i.e., hybridization to filter-bound DNA in 0.5 M NaHPO₄, 7% sodium dodecyl sulfate (SDS), 1 mM EDTA at 65°C, and washing in 0.1X SSC/0.1% SDS at 68°C), and moderately stringent conditions (i.e., washing in 0.2X SSC/0.1% SDS at 42°C). Other exemplary hybridization conditions are described herein in the examples.

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In instances of hybridization of deoxyoligonucleotides, additional exemplary stringent hybridization conditions include washing in 6X SSC/0.05% sodium pyrophosphate at 37°C (for 14-base oligonucleotides), 48°C (for 17-base oligos), 55°C (for 20-base oligonucleotides), and 60°C (for 23-base oligonucleotides).

As used herein, "substantially equivalent" can refer both to nucleotide and amino acid sequences, for example a mutant sequence, that varies from a reference sequence by one or more substitutions, deletions, or additions, the net effect of which does not result in an adverse functional dissimilarity between the reference and subject sequences. Typically, such a substantially equivalent sequence varies from one of those listed herein by no more than about 35% (i.e., the number of individual residue substitutions, additions, and/or deletions in a substantially equivalent sequence, as compared to the corresponding reference sequence, divided by the total number of residues in the substantially equivalent sequence is about 0.35 or less). Such a sequence is said to have 65% sequence identity to the listed sequence. In one embodiment, a substantially equivalent, e.g., mutant, sequence of the invention varies from a listed sequence by no more than 30% (70% sequence identity); in a variation of this embodiment, by no more than 25% (75% sequence identity); and in a further variation of this embodiment, by no more than 20% (80% sequence identity) and in a further variation of this embodiment, by no more than 10% (90% sequence identity) and in a further variation of this embodiment, by no more that 5% (95% sequence identity). Substantially equivalent, e.g., mutant, amino acid sequences according to the invention preferably have at least 80% sequence identity with a listed amino acid sequence, more preferably at least 85% sequence identity, more preferably at least 90% sequence identity, more preferably at least 95% identity, more preferably at least 98% identity, and most preferably at least 99% identity. Substantially equivalent nucleotide sequences of the invention can have lower percent sequence identities, taking into account, for example, the redundancy or degeneracy of the genetic code. Preferably, nucleotide sequence has at least about 65% identity, more preferably at least about 75% identity, more preferably at least about 80% sequence identity, more preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, and most preferably at least about 95% identity, more preferably at least about 98% sequence identity, and most preferably at least about 99% sequence identity. For the purposes of the present invention, sequences having substantially equivalent biological activity and substantially equivalent expression characteristics are considered substantially equivalent. For the purposes of determining equivalence, truncation of the mature sequence

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(e.g., via a mutation which creates a spurious stop codon) should be disregarded. Sequence identity may be determined, e.g., using the Jotun Hein method (Hein, J. (1990) Methods Enzymol. 183:626-645). Identity between sequences can also be determined by other methods known in the art, e.g. by varying hybridization conditions.

The term "totipotent" refers to the capability of a cell to differentiate into all of the cell types of an adult organism.

The term "transformation" means introducing DNA into a suitable host cell so that the DNA is replicable, either as an extrachromosomal element, or by chromosomal integration. The term "transfection" refers to the taking up of an expression vector by a suitable host cell, whether or not any coding sequences are in fact expressed. The term "infection" refers to the introduction of nucleic acids into a suitable host cell by use of a virus or viral vector.

As used herein, an "uptake modulating fragment," UMF, means a series of nucleotides which mediate the uptake of a linked DNA fragment into a cell. UMFs can be readily identified using known UMFs as a target sequence or target motif with the computer-based systems described below. The presence and activity of a UMF can be confirmed by attaching the suspected UMF to a marker sequence. The resulting nucleic acid molecule is then incubated with an appropriate host under appropriate conditions and the uptake of the marker sequence is determined. As described above, a UMF will increase the frequency of uptake of a linked marker sequence.

Each of the above terms is meant to encompass all that is described for each, unless the context dictates otherwise.

4.2 NUCLEIC ACIDS OF THE INVENTION

Nucleotide sequences of the invention are set forth in the Sequence Listing.

The isolated polynucleotides of the invention include a polynucleotide comprising the nucleotide sequences of SEQ ID NO: 1-93; a polynucleotide encoding any one of the peptide sequences of SEQ ID NO: 94-186; and a polynucleotide comprising the nucleotide sequence encoding the mature protein coding sequence of the polypeptides of any one of SEQ ID NO: 94-186. The polynucleotides of the present invention also include, but are not limited to, a polynucleotide that hybridizes under stringent conditions to (a) the complement of any of the nucleotides sequences of SEQ ID NO: 1-93; (b) nucleotide sequences encoding any one of the amino acid sequences set forth in the Sequence Listing as SEQ ID NO: 94-186; (c) a polynucleotide which is an allelic variant of any polynucleotide recited above; (d) a

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polynucleotide which encodes a species homolog of any of the proteins recited above; or (e) a polynucleotide that encodes a polypeptide comprising a specific domain or truncation of the polypeptides of SEQ ID NO: 94-186. Domains of interest may depend on the nature of the encoded polypeptide; e.g., domains in receptor-like polypeptides include ligand-binding, extracellular, transmembrane, or cytoplasmic domains, or combinations thereof; domains in immunoglobulin-like proteins include the variable immunoglobulin-like domains; domains in enzyme-like polypeptides include catalytic and substrate binding domains; and domains in ligand polypeptides include receptor-binding domains.

The polynucleotides of the invention include naturally occurring or wholly or partially synthetic DNA, e.g., cDNA and genomic DNA, and RNA, e.g., mRNA. The polynucleotides may include all of the coding region of the cDNA or may represent a portion of the coding region of the cDNA.

The present invention also provides genes corresponding to the cDNA sequences disclosed herein. The corresponding genes can be isolated in accordance with known methods using the sequence information disclosed herein. Such methods include the preparation of probes or primers from the disclosed sequence information for identification and/or amplification of genes in appropriate genomic libraries or other sources of genomic materials. Further 5' and 3' sequence can be obtained using methods known in the art. For example, full length cDNA or genomic DNA that corresponds to any of the polynucleotides of SEQ ID NO: 1-93 can be obtained by screening appropriate cDNA or genomic DNA libraries under suitable hybridization conditions using any of the polynucleotides of SEQ ID NO: 1-93 or a portion thereof as a probe. Alternatively, the polynucleotides of SEQ ID NO: 1-93 may be used as the basis for suitable primer(s) that allow identification and/or amplification of genes in appropriate genomic DNA or cDNA libraries.

The nucleic acid sequences of the invention can be assembled from ESTs and sequences (including cDNA and genomic sequences) obtained from one or more public databases, such as dbEST, gbpri, and UniGene. The EST sequences can provide identifying sequence information, representative fragment or segment information, or novel segment information for the full-length gene.

The polynucleotides of the invention also provide polynucleotides including nucleotide sequences that are substantially equivalent to the polynucleotides recited above. Polynucleotides according to the invention can have, e.g., at least about 65%, at least about 70%, at least about 80%, 81%, 82%, 83%, 84%, more typically at least

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about 85%, 86%, 87%, 88%, 89%, more typically at least about 90%, 91%, 92%, 93%, 94%, and even more typically at least about 95%, 96%, 97%, 98%, 99%, sequence identity to a polynucleotide recited above.

Included within the scope of the nucleic acid sequences of the invention are nucleic acid sequence fragments that hybridize under stringent conditions to any of the nucleotide sequences of SEQ ID NO: 1-93, or complements thereof, which fragment is greater than about 5 nucleotides, preferably 7 nucleotides, more preferably greater than 9 nucleotides and most preferably greater than 17 nucleotides. Fragments of, e.g. 15, 17, or 20 nucleotides or more that are selective for (i.e. specifically hybridize to) any one of the polynucleotides of the invention are contemplated. Probes capable of specifically hybridizing to a polynucleotide can differentiate polynucleotide sequences of the invention from other polynucleotide sequences in the same family of genes or can differentiate human genes from genes of other species, and are preferably based on unique nucleotide sequences.

The sequences falling within the scope of the present invention are not limited to these specific sequences, but also include allelic and species variations thereof. Allelic and species variations can be routinely determined by comparing the sequence provided in SEQ ID NO: 1-93, a representative fragment thereof, or a nucleotide sequence at least 90% identical, preferably 95% identical, to SEQ ID NO: 1-93 with a sequence from another isolate of the same species. Furthermore, to accommodate codon variability, the invention includes nucleic acid molecules coding for the same amino acid sequences as do the specific ORFs disclosed herein. In other words, in the coding region of an ORF, substitution of one codon for another codon that encodes the same amino acid is expressly contemplated.

The nearest neighbor or homology result for the nucleic acids of the present invention, including SEQ ID NO: 1-93, can be obtained by searching a database using an algorithm or a program. Preferably, a BLAST which stands for Basic Local Alignment Search Tool is used to search for local sequence alignments (Altshul, S.F. J Mol. Evol. 36 290-300 (1993) and Altschul S.F. et al. J. Mol. Biol. 21:403-410 (1990)). Alternatively a FASTA version 3 search against Genpept, using Fastxy algorithm.

Species homologs (or orthologs) of the disclosed polynucleotides and proteins are also provided by the present invention. Species homologs may be isolated and identified by making suitable probes or primers from the sequences provided herein and screening a suitable nucleic acid source from the desired species.

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The invention also encompasses allelic variants of the disclosed polynucleotides or proteins; that is, naturally-occurring alternative forms of the isolated polynucleotide which also encode proteins which are identical, homologous or related to that encoded by the polynucleotides.

The nucleic acid sequences of the invention are further directed to sequences which encode variants of the described nucleic acids. These amino acid sequence variants may be prepared by methods known in the art by introducing appropriate nucleotide changes into a native or variant polynucleotide. There are two variables in the construction of amino acid sequence variants: the location of the mutation and the nature of the mutation. Nucleic acids encoding the amino acid sequence variants are preferably constructed by mutating the polynucleotide to encode an amino acid sequence that does not occur in nature. These nucleic acid alterations can be made at sites that differ in the nucleic acids from different species (variable positions) or in highly conserved regions (constant regions). Sites at such locations will typically be modified in series, e.g., by substituting first with conservative choices (e.g., hydrophobic amino acid to a different hydrophobic amino acid) and then with more distant choices (e.g., hydrophobic amino acid to a charged amino acid), and then deletions or insertions may be made at the target site. Amino acid sequence deletions generally range from about 1 to 30 residues, preferably about 1 to 10 residues, and are typically contiguous. Amino acid insertions include amino- and/or carboxyl-terminal fusions ranging in length from one to one hundred or more residues, as well as intrasequence insertions of single or multiple amino acid residues. Intrasequence insertions may range generally from about 1 to 10 amino residues, preferably from 1 to 5 residues. Examples of terminal insertions include the heterologous signal sequences necessary for secretion or for intracellular targeting in different host cells and sequences such as FLAG or poly-histidine sequences useful for purifying the expressed protein.

In a preferred method, polynucleotides encoding the novel amino acid sequences are changed via site-directed mutagenesis. This method uses oligonucleotide sequences to alter a polynucleotide to encode the desired amino acid variant, as well as sufficient adjacent nucleotides on both sides of the changed amino acid to form a stable duplex on either side of the site of being changed. In general, the techniques of site-directed mutagenesis are well known to those of skill in the art and this technique is exemplified by publications such as, Edelman et al., *DNA* 2:183 (1983). A versatile and efficient method for producing site-specific changes in a polynucleotide sequence was published by Zoller and Smith,

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Nucleic Acids Res. 10:6487-6500 (1982). PCR may also be used to create amino acid sequence variants of the novel nucleic acids. When small amounts of template DNA are used as starting material, primer(s) that differs slightly in sequence from the corresponding region in the template DNA can generate the desired amino acid variant. PCR amplification results in a population of product DNA fragments that differ from the polynucleotide template encoding the polypeptide at the position specified by the primer. The product DNA fragments replace the corresponding region in the plasmid and this gives a polynucleotide encoding the desired amino acid variant.

A further technique for generating amino acid variants is the cassette mutagenesis technique described in Wells et al., *Gene* 34:315 (1985); and other mutagenesis techniques well known in the art, such as, for example, the techniques in Sambrook et al., supra, and *Current Protocols in Molecular Biology*, Ausubel et al. Due to the inherent degeneracy of the genetic code, other DNA sequences which encode substantially the same or a functionally equivalent amino acid sequence may be used in the practice of the invention for the cloning and expression of these novel nucleic acids. Such DNA sequences include those which are capable of hybridizing to the appropriate novel nucleic acid sequence under stringent conditions.

Polynucleotides encoding preferred polypeptide truncations of the invention can be used to generate polynucleotides encoding chimeric or fusion proteins comprising one or more domains of the invention and heterologous protein sequences.

The polynucleotides of the invention additionally include the complement of any of the polynucleotides recited above. The polynucleotide can be DNA (genomic, cDNA, amplified, or synthetic) or RNA. Methods and algorithms for obtaining such polynucleotides are well known to those of skill in the art and can include, for example, methods for determining hybridization conditions that can routinely isolate polynucleotides of the desired sequence identities.

In accordance with the invention, polynucleotide sequences comprising the mature protein coding sequences corresponding to any one of SEQ ID NO: 1-93, or functional equivalents thereof, may be used to generate recombinant DNA molecules that direct the expression of that nucleic acid, or a functional equivalent thereof, in appropriate host cells. Also included are the cDNA inserts of any of the clones identified herein.

A polynucleotide according to the invention can be joined to any of a variety of other nucleotide sequences by well-established recombinant DNA techniques (see Sambrook J et

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al. (1989) Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Laboratory, NY). Useful nucleotide sequences for joining to polynucleotides include an assortment of vectors, e.g., plasmids, cosmids, lambda phage derivatives, phagemids, and the like, that are well known in the art. Accordingly, the invention also provides a vector including a polynucleotide of the invention and a host cell containing the polynucleotide. In general, the vector contains an origin of replication functional in at least one organism, convenient restriction endonuclease sites, and a selectable marker for the host cell. Vectors according to the invention include expression vectors, replication vectors, probe generation vectors, and sequencing vectors. A host cell according to the invention can be a prokaryotic or eukaryotic cell and can be a unicellular organism or part of a multicellular organism.

The present invention further provides recombinant constructs comprising a nucleic acid having any of the nucleotide sequences of SEQ ID NO: 1-93 or a fragment thereof or any other polynucleotides of the invention. In one embodiment, the recombinant constructs of the present invention comprise a vector, such as a plasmid or viral vector, into which a nucleic acid having any of the nucleotide sequences of SEQ ID NO: 1-93 or a fragment thereof is inserted, in a forward or reverse orientation. In the case of a vector comprising one of the ORFs of the present invention, the vector may further comprise regulatory sequences, including for example, a promoter, operably linked to the ORF. Large numbers of suitable vectors and promoters are known to those of skill in the art and are commercially available for generating the recombinant constructs of the present invention. The following vectors are provided by way of example. Bacterial: pBs, phagescript, PsiX174, pBluescript SK, pBs KS, pNH8a, pNH16a, pNH18a, pNH46a (Stratagene); pTrc99A, pKK223-3, pKK233-3, pDR540, pRIT5 (Pharmacia). Eukaryotic: pWLneo, pSV2cat, pOG44, PXTI, pSG (Stratagene) pSVK3, pBPV, pMSG, pSVL (Pharmacia).

The isolated polynucleotide of the invention may be operably linked to an expression control sequence such as the pMT2 or pED expression vectors disclosed in Kaufman et al., Nucleic Acids Res. 19, 4485-4490 (1991), in order to produce the protein recombinantly. Many suitable expression control sequences are known in the art. General methods of expressing recombinant proteins are also known and are exemplified in R. Kaufman, Methods in Enzymology 185, 537-566 (1990). As defined herein "operably linked" means that the isolated polynucleotide of the invention and an expression control sequence are situated within a vector or cell in such a way that the protein is expressed by a host cell which has been transformed (transfected) with the ligated polynucleotide/expression control sequence.

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Promoter regions can be selected from any desired gene using CAT (chloramphenicol transferase) vectors or other vectors with selectable markers. Two appropriate vectors are pKK232-8 and pCM7. Particular named bacterial promoters include lacI, lacZ, T3, T7, gpt, lambda PR, and trc. Eukaryotic promoters include CMV immediate early, HSV thymidine kinase, early and late SV40, LTRs from retrovirus, and mouse metallothionein-I. Selection of the appropriate vector and promoter is well within the level of ordinary skill in the art. Generally, recombinant expression vectors will include origins of replication and selectable markers permitting transformation of the host cell, e.g., the ampicillin resistance gene of E. coli and S. cerevisiae TRP1 gene, and a promoter derived from a highly-expressed gene to direct transcription of a downstream structural sequence. Such promoters can be derived from operons encoding glycolytic enzymes such as 3-phosphoglycerate kinase (PGK), a-factor, acid phosphatase, or heat shock proteins, among others. The heterologous structural sequence is assembled in appropriate phase with translation initiation and termination sequences, and preferably, a leader sequence capable of directing secretion of translated protein into the periplasmic space or extracellular medium. Optionally, the heterologous sequence can encode a fusion protein including an amino terminal identification peptide imparting desired characteristics, e.g., stabilization or simplified purification of expressed recombinant product. Useful expression vectors for bacterial use are constructed by inserting a structural DNA sequence encoding a desired protein together with suitable translation initiation and termination signals in operable reading phase with a functional promoter. The vector will comprise one or more phenotypic selectable markers and an origin of replication to ensure maintenance of the vector and to, if desirable, provide amplification within the host. Suitable prokaryotic hosts for transformation include E. coli, Bacillus subtilis, Salmonella typhimurium and various species within the genera Pseudomonas, Streptomyces, and Staphylococcus, although others may also be employed as a matter of choice.

As a representative but non-limiting example, useful expression vectors for bacterial use can comprise a selectable marker and bacterial origin of replication derived from commercially available plasmids comprising genetic elements of the well known cloning vector pBR322 (ATCC 37017). Such commercial vectors include, for example, pKK223-3 (Pharmacia Fine Chemicals, Uppsala, Sweden) and GEM 1 (Promega Biotech, Madison, WI, USA). These pBR322 "backbone" sections are combined with an appropriate promoter and the structural sequence to be expressed. Following transformation of a suitable host strain and growth of the host strain to an appropriate cell density, the selected promoter is induced

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or derepressed by appropriate means (e.g., temperature shift or chemical induction) and cells are cultured for an additional period. Cells are typically harvested by centrifugation, disrupted by physical or chemical means, and the resulting crude extract retained for further purification.

Polynucleotides of the invention can also be used to induce immune responses. For example, as described in Fan et al., *Nat. Biotech.* 17:870-872 (1999), incorporated herein by reference, nucleic acid sequences encoding a polypeptide may be used to generate antibodies against the encoded polypeptide following topical administration of naked plasmid DNA or following injection, and preferably intramuscular injection of the DNA. The nucleic acid sequences are preferably inserted in a recombinant expression vector and may be in the form of naked DNA.

4.3 ANTISENSE NUCLEIC ACIDS

Another aspect of the invention pertains to isolated antisense nucleic acid molecules that are hybridizable to or complementary to the nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO: 1-93, or fragments, analogs or derivatives thereof. An "antisense" nucleic acid comprises a nucleotide sequence that is complementary to a "sense" nucleic acid encoding a protein, e.g., complementary to the coding strand of a double-stranded cDNA molecule or complementary to an mRNA sequence. In specific aspects, antisense nucleic acid molecules are provided that comprise a sequence complementary to at least about 10, 25, 50, 100, 250 or 500 nucleotides or an entire coding strand, or to only a portion thereof. Nucleic acid molecules encoding fragments, homologs, derivatives and analogs of a protein of any of SEQ ID NO: 94-186 or antisense nucleic acids complementary to a nucleic acid sequence of SEQ ID NO: 1-93 are additionally provided.

In one embodiment, an antisense nucleic acid molecule is antisense to a "coding region" of the coding strand of a nucleotide sequence of the invention. The term "coding region" refers to the region of the nucleotide sequence comprising codons which are translated into amino acid residues. In another embodiment, the antisense nucleic acid molecule is antisense to a "noncoding region" of the coding strand of a nucleotide sequence of the invention. The term "noncoding region" refers to 5' and 3' sequences which flank the coding region that are not translated into amino acids (*i.e.*, also referred to as 5' and 3' untranslated regions).

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Given the coding strand sequences encoding a nucleic acid disclosed herein (e.g., SEQ ID NO: 1-93), antisense nucleic acids of the invention can be designed according to the rules of Watson and Crick or Hoogsteen base pairing. The antisense nucleic acid molecule can be complementary to the entire coding region of an mRNA, but more preferably is an oligonucleotide that is antisense to only a portion of the coding or noncoding region of a mRNA. For example, the antisense oligonucleotide can be complementary to the region surrounding the translation start site of an mRNA. An antisense oligonucleotide can be, for example, about 5, 10, 15, 20, 25, 30, 35, 40, 45 or 50 nucleotides in length. An antisense nucleic acid of the invention can be constructed using chemical synthesis or enzymatic ligation reactions using procedures known in the art. For example, an antisense nucleic acid (e.g., an antisense oligonucleotide) can be chemically synthesized using naturally occurring nucleotides or variously modified nucleotides designed to increase the biological stability of the molecules or to increase the physical stability of the duplex formed between the antisense and sense nucleic acids, e.g., phosphorothioate derivatives and acridine substituted nucleotides can be used.

Examples of modified nucleotides that can be used to generate the antisense nucleic acid include: 5-fluorouracil, 5-bromouracil, 5-chlorouracil, 5-iodouracil, hypoxanthine, xanthine, 4-acetylcytosine, 5-(carboxyhydroxylmethyl) uracil, 5-carboxymethylaminomethyl-2-thiouridine, 5-carboxymethylaminomethyluracil, dihydrouracil, beta-D-galactosylqueosine, inosine, N6-isopentenyladenine, 1-methylguanine, 1-methylinosine, 2,2-dimethylguanine, 2-methyladenine, 2-methylguanine, 3-methylcytosine, 5-methylcytosine, N6-adenine, 7-methylguanine, 5-methylaminomethyluracil, 5-methoxyaminomethyl-2-thiouracil, beta-D-mannosylqueosine, 5'-methoxycarboxymethyluracil, 5-methoxyuracil, 2-methylthio-N6-isopentenyladenine, uracil-5-oxyacetic acid (v), wybutoxosine, pseudouracil, queosine, 2-thiocytosine, 5-methyl-2-thiouracil, 2-thiouracil, 4-thiouracil, 5-methyluracil, uracil-5-oxyacetic acid methylester, uracil-5-oxyacetic acid (v), 5-methyl-2-thiouracil, 3-(3-amino-3-N-2-carboxypropyl) uracil, (acp3)w, and 2,6-diaminopurine. Alternatively, the antisense nucleic acid can be produced biologically using an expression vector into which a nucleic acid has been subcloned in an antisense orientation (i.e., RNA transcribed from the inserted nucleic acid will be of an antisense orientation to a target nucleic acid of interest, described further in the following subsection).

The antisense nucleic acid molecules of the invention are typically administered to a subject or generated *in situ* such that they hybridize with or bind to cellular mRNA and/or

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genomic DNA encoding a protein according to the invention to thereby inhibit expression of the protein, e.g., by inhibiting transcription and/or translation. The hybridization can be by conventional nucleotide complementarity to form a stable duplex, or, for example, in the case of an antisense nucleic acid molecule that binds to DNA duplexes, through specific interactions in the major groove of the double helix. An example of a route of administration of antisense nucleic acid molecules of the invention includes direct injection at a tissue site. Alternatively, antisense nucleic acid molecules can be modified to target selected cells and then administered systemically. For example, for systemic administration, antisense molecules can be modified such that they specifically bind to receptors or antigens expressed on a selected cell surface, e.g., by linking the antisense nucleic acid molecules to peptides or antibodies that bind to cell surface receptors or antigens. The antisense nucleic acid molecules can also be delivered to cells using the vectors described herein. To achieve sufficient intracellular concentrations of antisense molecules, vector constructs in which the antisense nucleic acid molecule is placed under the control of a strong pol II or pol III promoter are preferred.

In yet another embodiment, the antisense nucleic acid molecule of the invention is an α-anomeric nucleic acid molecule. An α-anomeric nucleic acid molecule forms specific double-stranded hybrids with complementary RNA in which, contrary to the usual β-units, the strands run parallel to each other (Gaultier et al. (1987) Nucleic Acids Res 15: 6625-6641). The antisense nucleic acid molecule can also comprise a 2'-o-methylribonucleotide (Inoue et al. (1987) Nucleic Acids Res 15: 6131-6148) or a chimeric RNA -DNA analogue (Inoue et al. (1987) FEBS Lett 215: 327-330).

4.4 RIBOZYMES AND PNA MOIETIES

In still another embodiment, an antisense nucleic acid of the invention is a ribozyme. Ribozymes are catalytic RNA molecules with ribonuclease activity that are capable of cleaving a single-stranded nucleic acid, such as an mRNA, to which they have a complementary region. Thus, ribozymes (e.g., hammerhead ribozymes (described in Haselhoff and Gerlach (1988) Nature 334:585-591)) can be used to catalytically cleave a mRNA transcripts to thereby inhibit translation of a mRNA. A ribozyme having specificity for a nucleic acid of the invention can be designed based upon the nucleotide sequence of a DNA disclosed herein (i.e., SEQ ID NO: 1-93). For example, a derivative of a Tetrahymena L-19 IVS RNA can be constructed in which the nucleotide sequence of the active site is

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complementary to the nucleotide sequence to be cleaved in an mRNA of SEQ ID NO: 1-93 (see, e.g., Cech et al. U.S. Pat. No. 4,987,071; and Cech et al. U.S. Pat. No. 5,116,742). Alternatively, polynucleotides of the invention can be used to select a catalytic RNA having a specific ribonuclease activity from a pool of RNA molecules. See, e.g., Bartel et al., (1993) Science 261:1411-1418.

Alternatively, gene expression can be inhibited by targeting nucleotide sequences complementary to the regulatory region (e.g., promoter and/or enhancers) to form triple helical structures that prevent transcription of the gene in target cells. See generally, Helene. (1991) Anticancer Drug Des. 6: 569-84; Helene. et al. (1992) Ann. N.Y. Acad. Sci. 660:27-36; and Maher (1992) Bioassays 14: 807-15.

In various embodiments, the nucleic acids of the invention can be modified at the base moiety, sugar moiety or phosphate backbone to improve, e.g., the stability, hybridization, or solubility of the molecule. For example, the deoxyribose phosphate backbone of the nucleic acids can be modified to generate peptide nucleic acids (see Hyrup et al. (1996) Bioorg Med Chem 4: 5-23). As used herein, the terms "peptide nucleic acids" or "PNAs" refer to nucleic acid mimics, e.g., DNA mimics, in which the deoxyribose phosphate backbone is replaced by a pseudopeptide backbone and only the four natural nucleobases are retained. The neutral backbone of PNAs has been shown to allow for specific hybridization to DNA and RNA under conditions of low ionic strength. The synthesis of PNA oligomers can be performed using standard solid phase peptide synthesis protocols as described in Hyrup et al. (1996) above; Perry-O'Keefe et al. (1996) PNAS 93: 14670-675.

PNAs of the invention can be used in therapeutic and diagnostic applications. For example, PNAs can be used as antisense or antigene agents for sequence-specific modulation of gene expression by, e.g., inducing transcription or translation arrest or inhibiting replication. PNAs of the invention can also be used, e.g., in the analysis of single base pair mutations in a gene by, e.g., PNA directed PCR clamping; as artificial restriction enzymes when used in combination with other enzymes, e.g., S1 nucleases (Hyrup B. (1996) above); or as probes or primers for DNA sequence and hybridization (Hyrup et al. (1996), above; Perry-O'Keefe (1996), above).

In another embodiment, PNAs of the invention can be modified, e.g., to enhance their stability or cellular uptake, by attaching lipophilic or other helper groups to PNA, by the formation of PNA-DNA chimeras, or by the use of liposomes or other techniques of drug delivery known in the art. For example, PNA-DNA chimeras can be generated that may

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combine the advantageous properties of PNA and DNA. Such chimeras allow DNA recognition enzymes, e.g., RNase H and DNA polymerases, to interact with the DNA portion while the PNA portion would provide high binding affinity and specificity. PNA-DNA chimeras can be linked using linkers of appropriate lengths selected in terms of base stacking, number of bonds between the nucleobases, and orientation (Hyrup (1996) above). The synthesis of PNA-DNA chimeras can be performed as described in Hyrup (1996) above and Finn et al. (1996) Nucl Acids Res 24: 3357-63. For example, a DNA chain can be synthesized on a solid support using standard phosphoramidite coupling chemistry, and modified nucleoside analogs, e.g., 5'-(4-methoxytrityl)amino-5'-deoxy-thymidine phosphoramidite, can be used between the PNA and the 5' end of DNA (Mag et al. (1989) Nucl Acid Res 17: 5973-88). PNA monomers are then coupled in a stepwise manner to produce a chimeric molecule with a 5' PNA segment and a 3' DNA segment (Finn et al. (1996) above). Alternatively, chimeric molecules can be synthesized with a 5' DNA segment and a 3' PNA segment. See, Petersen et al. (1975) Bioorg Med Chem Lett 5: 1119-11124.

In other embodiments, the oligonucleotide may include other appended groups such as peptides (e.g., for targeting host cell receptors in vivo), or agents facilitating transport across the cell membrane (see, e.g., Letsinger et al., 1989, Proc. Natl. Acad. Sci. U.S.A. 86:6553-6556; Lemaitre et al., 1987, Proc. Natl. Acad. Sci. 84:648-652; PCT Publication No. W088/09810) or the blood-brain barrier (see, e.g., PCT Publication No. W089/10134). In addition, oligonucleotides can be modified with hybridization triggered cleavage agents (See, e.g., Krol et al., 1988, BioTechniques 6:958-976) or intercalating agents. (See, e.g., Zon, 1988, Pharm. Res. 5: 539-549). To this end, the oligonucleotide may be conjugated to another molecule, e.g., a peptide, a hybridization triggered cross-linking agent, a transport agent, a hybridization-triggered cleavage agent, etc.

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4.5 HOSTS

The present invention further provides host cells genetically engineered to contain the polynucleotides of the invention. For example, such host cells may contain nucleic acids of the invention introduced into the host cell using known transformation, transfection or infection methods. The present invention still further provides host cells genetically engineered to express the polynucleotides of the invention, wherein such polynucleotides are in operative association with a regulatory sequence heterologous to the host cell which drives expression of the polynucleotides in the cell.

Knowledge of nucleic acid sequences allows for modification of cells to permit, or increase, expression of endogenous polypeptide. Cells can be modified (e.g., by homologous recombination) to provide increased polypeptide expression by replacing, in whole or in part, the naturally occurring promoter with all or part of a heterologous promoter so that the cells express the polypeptide at higher levels. The heterologous promoter is inserted in such a manner that it is operatively linked to the encoding sequences. See, for example, PCT International Publication No. WO94/12650, PCT International Publication No. WO92/20808, and PCT International Publication No. WO91/09955. It is also contemplated that, in addition to heterologous promoter DNA, amplifiable marker DNA (e.g., ada, dhfr, and the multifunctional CAD gene which encodes carbamyl phosphate synthase, aspartate transcarbamylase, and dihydroorotase) and/or intron DNA may be inserted along with the heterologous promoter DNA. If linked to the coding sequence, amplification of the marker DNA by standard selection methods results in co-amplification of the desired protein coding sequences in the cells.

The host cell can be a higher eukaryotic host cell, such as a mammalian cell, a lower eukaryotic host cell, such as a yeast cell, or the host cell can be a prokaryotic cell, such as a bacterial cell. Introduction of the recombinant construct into the host cell can be effected by calcium phosphate transfection, DEAE-dextran mediated transfection, or electroporation (Davis, L. et al., *Basic Methods in Molecular Biology* (1986)). The host cells containing one of the polynucleotides of the invention, can be used in conventional manners to produce the gene product encoded by the isolated fragment (in the case of an ORF) or can be used to produce a heterologous protein under the control of the EMF.

Any host/vector system can be used to express one or more of the ORFs of the present invention. These include, but are not limited to, eukaryotic hosts such as HeLa cells, Cv-1 cell, COS cells, 293 cells, and Sf9 cells, as well as prokaryotic host such as *E. coli* and *B. subtilis*. The most preferred cells are those which do not normally express the particular polypeptide or protein or which expresses the polypeptide or protein at low natural level. Mature proteins can be expressed in mammalian cells, yeast, bacteria, or other cells under the control of appropriate promoters. Cell-free translation systems can also be employed to produce such proteins using RNAs derived from the DNA constructs of the present invention. Appropriate cloning and expression vectors for use with prokaryotic and eukaryotic hosts are described by Sambrook, et al., in Molecular Cloning: A Laboratory Manual, Second Edition,

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Cold Spring Harbor, New York (1989), the disclosure of which is hereby incorporated by reference.

. Various mammalian cell culture systems can also be employed to express recombinant protein. Examples of mammalian expression systems include the COS-7 lines of monkey kidney fibroblasts, described by Gluzman, Cell 23:175 (1981). Other cell lines capable of expressing a compatible vector are, for example, the C127, monkey COS cells, Chinese Hamster Ovary (CHO) cells, human kidney 293 cells, human epidermal A431 cells, human Colo205 cells, 3T3 cells, CV-1 cells, other transformed primate cell lines, normal diploid cells, cell strains derived from in vitro culture of primary tissue, primary explants, HeLa cells, mouse L cells, BHK, HL-60, U937, HaK or Jurkat cells. Mammalian expression vectors will comprise an origin of replication, a suitable promoter and also any necessary ribosome binding sites, polyadenylation site, splice donor and acceptor sites, transcriptional termination sequences, and 5' flanking nontranscribed sequences. DNA sequences derived from the SV40 viral genome, for example, SV40 origin, early promoter, enhancer, splice, and polyadenylation sites may be used to provide the required nontranscribed genetic elements. Recombinant polypeptides and proteins produced in bacterial culture are usually isolated by initial extraction from cell pellets, followed by one or more salting-out, aqueous ion exchange or size exclusion chromatography steps. Protein refolding steps can be used, as necessary, in completing configuration of the mature protein. Finally, high performance liquid chromatography (HPLC) can be employed for final purification steps. Microbial cells employed in expression of proteins can be disrupted by any convenient method, including freeze-thaw cycling, sonication, mechanical disruption, or use of cell lysing agents.

Alternatively, it may be possible to produce the protein in lower eukaryotes such as yeast or insects or in prokaryotes such as bacteria. Potentially suitable yeast strains include Saccharomyces cerevisiae, Schizosaccharomyces pombe, Kluyveromyces strains, Candida, or any yeast strain capable of expressing heterologous proteins. Potentially suitable bacterial strains include Escherichia coli, Bacillus subtilis, Salmonella typhimurium, or any bacterial strain capable of expressing heterologous proteins. If the protein is made in yeast or bacteria, it may be necessary to modify the protein produced therein, for example by phosphorylation or glycosylation of the appropriate sites, in order to obtain the functional protein. Such covalent attachments may be accomplished using known chemical or enzymatic methods.

In another embodiment of the present invention, cells and tissues may be engineered to express an endogenous gene comprising the polynucleotides of the invention under the

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control of inducible regulatory elements, in which case the regulatory sequences of the endogenous gene may be replaced by homologous recombination. As described herein, gene targeting can be used to replace a gene's existing regulatory region with a regulatory sequence isolated from a different gene or a novel regulatory sequence synthesized by genetic engineering methods. Such regulatory sequences may be comprised of promoters, enhancers, scaffold-attachment regions, negative regulatory elements, transcriptional initiation sites, regulatory protein binding sites or combinations of said sequences. Alternatively, sequences which affect the structure or stability of the RNA or protein produced may be replaced, removed, added, or otherwise modified by targeting. These sequence include polyadenylation signals, mRNA stability elements, splice sites, leader sequences for enhancing or modifying transport or secretion properties of the protein, or other sequences which alter or improve the function or stability of protein or RNA molecules.

The targeting event may be a simple insertion of the regulatory sequence, placing the gene under the control of the new regulatory sequence, e.g., inserting a new promoter or enhancer or both upstream of a gene. Alternatively, the targeting event may be a simple deletion of a regulatory element, such as the deletion of a tissue-specific negative regulatory element. Alternatively, the targeting event may replace an existing element; for example, a tissue-specific enhancer can be replaced by an enhancer that has broader or different cell-type specificity than the naturally occurring elements. Here, the naturally occurring sequences are deleted and new sequences are added. In all cases, the identification of the targeting event may be facilitated by the use of one or more selectable marker genes that are contiguous with the targeting DNA, allowing for the selection of cells in which the exogenous DNA has integrated into the host cell genome. The identification of the targeting event may also be facilitated by the use of one or more marker genes exhibiting the property of negative selection, such that the negatively selectable marker is linked to the exogenous DNA, but configured such that the negatively selectable marker flanks the targeting sequence, and such that a correct homologous recombination event with sequences in the host cell genome does not result in the stable integration of the negatively selectable marker. Markers useful for this purpose include the Herpes Simplex Virus thymidine kinase (TK) gene or the bacterial xanthine-guanine phosphoribosyl-transferase (gpt) gene.

The gene targeting or gene activation techniques which can be used in accordance with this aspect of the invention are more particularly described in U.S. Patent No. 5,272,071 to Chappel; U.S. Patent No. 5,578,461 to Sherwin et al.; International Application No.

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PCT/US92/09627 (WO93/09222) by Selden et al.; and International Application No. PCT/US90/06436 (WO91/06667) by Skoultchi et al., each of which is incorporated by reference herein in its entirety.

4.6 POLYPEPTIDES OF THE INVENTION

The isolated polypeptides of the invention include, but are not limited to, a polypeptide comprising: the amino acid sequences set forth as any one of SEQ ID NO: 94-186 or an amino acid sequence encoded by any one of the nucleotide sequences SEQ ID NO: 1-93 or the corresponding full length or mature protein. Polypeptides of the invention also include polypeptides preferably with biological or immunological activity that are encoded by: (a) a polynucleotide having any one of the nucleotide sequences set forth in SEQ ID NO: 1-93 or (b) polynucleotides encoding any one of the amino acid sequences set forth as SEQ ID NO: 94-186 or (c) polynucleotides that hybridize to the complement of the polynucleotides of either (a) or (b) under stringent hybridization conditions. The invention also provides biologically active or immunologically active variants of any of the amino acid sequences set forth as SEQ ID NO: 94-186 or the corresponding full length or mature protein; and "substantial equivalents" thereof (e.g., with at least about 65%, at least about 70%, at least about 75%, at least about 80%, at least about 85%, 86%, 87%, 88%, 89%, at least about 90%, 91%, 92%, 93%, 94%, typically at least about 95%, 96%, 97%, more typically at least about 98%, or most typically at least about 99% amino acid identity) that retain biological activity. Polypeptides encoded by allelic variants may have a similar, increased, or decreased activity compared to polypeptides comprising SEQ ID NO: 94-186.

Fragments of the proteins of the present invention which are capable of exhibiting biological activity are also encompassed by the present invention. Fragments of the protein may be in linear form or they may be cyclized using known methods, for example, as described in H. U. Saragovi, et al., Bio/Technology 10, 773-778 (1992) and in R. S. McDowell, et al., J. Amer. Chem. Soc. 114, 9245-9253 (1992), both of which are incorporated herein by reference. Such fragments may be fused to carrier molecules such as immunoglobulins for many purposes, including increasing the valency of protein binding sites.

The present invention also provides both full-length and mature forms (for example, without a signal sequence or precursor sequence) of the disclosed proteins. The protein coding sequence is identified in the sequence listing by translation of the disclosed nucleotide

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sequences. The mature form of such protein may be obtained by expression of a full-length polynucleotide in a suitable mammalian cell or other host cell. The sequence of the mature form of the protein is also determinable from the amino acid sequence of the full-length form. Where proteins of the present invention are membrane bound, soluble forms of the proteins are also provided. In such forms, part or all of the regions causing the proteins to be membrane bound are deleted so that the proteins are fully secreted from the cell in which they are expressed.

Protein compositions of the present invention may further comprise an acceptable carrier, such as a hydrophilic, e.g., pharmaceutically acceptable, carrier.

The present invention further provides isolated polypeptides encoded by the nucleic acid fragments of the present invention or by degenerate variants of the nucleic acid fragments of the present invention. By "degenerate variant" is intended nucleotide fragments which differ from a nucleic acid fragment of the present invention (e.g., an ORF) by nucleotide sequence but, due to the degeneracy of the genetic code, encode an identical polypeptide sequence. Preferred nucleic acid fragments of the present invention are the ORFs that encode proteins.

A variety of methodologies known in the art can be utilized to obtain any one of the isolated polypeptides or proteins of the present invention. At the simplest level, the amino acid sequence can be synthesized using commercially available peptide synthesizers. The synthetically-constructed protein sequences, by virtue of sharing primary, secondary or tertiary structural and/or conformational characteristics with proteins may possess biological properties in common therewith, including protein activity. This technique is particularly useful in producing small peptides and fragments of larger polypeptides. Fragments are useful, for example, in generating antibodies against the native polypeptide. Thus, they may be employed as biologically active or immunological substitutes for natural, purified proteins in screening of therapeutic compounds and in immunological processes for the development of antibodies.

The polypeptides and proteins of the present invention can alternatively be purified from cells which have been altered to express the desired polypeptide or protein. As used herein, a cell is said to be altered to express a desired polypeptide or protein when the cell, through genetic manipulation, is made to produce a polypeptide or protein which it normally does not produce or which the cell normally produces at a lower level. One skilled in the art can readily adapt procedures for introducing and expressing either recombinant or synthetic

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sequences into eukaryotic or prokaryotic cells in order to generate a cell which produces one of the polypeptides or proteins of the present invention.

The invention also relates to methods for producing a polypeptide comprising growing a culture of host cells of the invention in a suitable culture medium, and purifying 5 the protein from the cells or the culture in which the cells are grown. For example, the methods of the invention include a process for producing a polypeptide in which a host cell containing a suitable expression vector that includes a polynucleotide of the invention is cultured under conditions that allow expression of the encoded polypeptide. The polypeptide can be recovered from the culture, conveniently from the culture medium, or from a lysate prepared from the host cells and further purified. Preferred embodiments include those in which the protein produced by such process is a full length or mature form of the protein.

In an alternative method, the polypeptide or protein is purified from bacterial cells which naturally produce the polypeptide or protein. One skilled in the art can readily follow known methods for isolating polypeptides and proteins in order to obtain one of the isolated polypeptides or proteins of the present invention. These include, but are not limited to, immunochromatography, HPLC, size-exclusion chromatography, ion-exchange chromatography, and immuno-affinity chromatography. See, e.g., Scopes, Protein Purification: Principles and Practice, Springer-Verlag (1994); Sambrook, et al., in Molecular Cloning: A Laboratory Manual; Ausubel et al., Current Protocols in Molecular Biology. Polypeptide fragments that retain biological/immunological activity include fragments comprising greater than about 100 amino acids, or greater than about 200 amino acids, and fragments that encode specific protein domains.

The purified polypeptides can be used in in vitro binding assays which are well known in the art to identify molecules which bind to the polypeptides. These molecules include but are not limited to, for e.g., small molecules, molecules from combinatorial libraries, antibodies or other proteins. The molecules identified in the binding assay are then tested for antagonist or agonist activity in in vivo tissue culture or animal models that are well known in the art. In brief, the molecules are titrated into a plurality of cell cultures or animals and then tested for either cell/animal death or prolonged survival of the animal/cells.

In addition, the peptides of the invention or molecules capable of binding to the peptides may be complexed with toxins, e.g., ricin or cholera, or with other compounds that are toxic to cells. The toxin-binding molecule complex is then targeted to a tumor or other cell by the specificity of the binding molecule for SEQ ID NO: 94-186.

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The protein of the invention may also be expressed as a product of transgenic animals, e.g., as a component of the milk of transgenic cows, goats, pigs, or sheep which are characterized by somatic or germ cells containing a nucleotide sequence encoding the protein.

The proteins provided herein also include proteins characterized by amino acid sequences similar to those of purified proteins but into which modification are naturally provided or deliberately engineered. For example, modifications, in the peptide or DNA sequence, can be made by those skilled in the art using known techniques. Modifications of interest in the protein sequences may include the alteration, substitution, replacement, insertion or deletion of a selected amino acid residue in the coding sequence. For example, one or more of the cysteine residues may be deleted or replaced with another amino acid to alter the conformation of the molecule. Techniques for such alteration, substitution, replacement, insertion or deletion are well known to those skilled in the art (see, e.g., U.S. Pat. No. 4,518,584). Preferably, such alteration, substitution, replacement, insertion or deletion retains the desired activity of the protein. Regions of the protein that are important for the protein function can be determined by various methods known in the art including the alanine-scanning method which involved systematic substitution of single or strings of amino acids with alanine, followed by testing the resulting alanine-containing variant for biological activity. This type of analysis determines the importance of the substituted amino acid(s) in biological activity. Regions of the protein that are important for protein function may be determined by the eMATRIX program.

Other fragments and derivatives of the sequences of proteins which would be expected to retain protein activity in whole or in part and are useful for screening or other immunological methodologies may also be easily made by those skilled in the art given the disclosures herein. Such modifications are encompassed by the present invention.

The protein may also be produced by operably linking the isolated polynucleotide of the invention to suitable control sequences in one or more insect expression vectors, and employing an insect expression system. Materials and methods for baculovirus/insect cell expression systems are commercially available in kit form from, e.g., Invitrogen, San Diego, Calif., U.S.A. (the MaxBatTM kit), and such methods are well known in the art, as described in Summers and Smith, Texas Agricultural Experiment Station Bulletin No. 1555 (1987), incorporated herein by reference. As used herein, an insect cell capable of expressing a polynucleotide of the present invention is "transformed."

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The protein of the invention may be prepared by culturing transformed host cells under culture conditions suitable to express the recombinant protein. The resulting expressed protein may then be purified from such culture (*i.e.*, from culture medium or cell extracts) using known purification processes, such as gel filtration and ion exchange chromatography. The purification of the protein may also include an affinity column containing agents which will bind to the protein; one or more column steps over such affinity resins as concanavalin A-agarose, heparin-toyopearlTM or Cibacrom blue 3GA SepharoseTM; one or more steps involving hydrophobic interaction chromatography using such resins as phenyl ether, butyl ether, or propyl ether; or immunoaffinity chromatography.

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Alternatively, the protein of the invention may also be expressed in a form which will facilitate purification. For example, it may be expressed as a fusion protein, such as those of maltose binding protein (MBP), glutathione-S-transferase (GST) or thioredoxin (TRX), or as a His tag. Kits for expression and purification of such fusion proteins are commercially available from New England BioLab (Beverly, Mass.), Pharmacia (Piscataway, N.J.) and Invitrogen, respectively. The protein can also be tagged with an epitope and subsequently purified by using a specific antibody directed to such epitope. One such epitope ("FLAG®") is commercially available from Kodak (New Haven, Conn.).

Finally, one or more reverse-phase high performance liquid chromatography (RP-HPLC) steps employing hydrophobic RP-HPLC media, e.g., silica gel having pendant methyl or other aliphatic groups, can be employed to further purify the protein. Some or all of the foregoing purification steps, in various combinations, can also be employed to provide a substantially homogeneous isolated recombinant protein. The protein thus purified is substantially free of other mammalian proteins and is defined in accordance with the present invention as an "isolated protein."

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The polypeptides of the invention include analogs (variants). This embraces fragments, as well as peptides in which one or more amino acids has been deleted, inserted, or substituted. Also, analogs of the polypeptides of the invention embrace fusions of the polypeptides or modifications of the polypeptides of the invention, wherein the polypeptide or analog is fused to another moiety or moieties, e.g., targeting moiety or another therapeutic agent. Such analogs may exhibit improved properties such as activity and/or stability. Examples of moieties which may be fused to the polypeptide or an analog include, for example, targeting moieties which provide for the delivery of polypeptide to pancreatic cells, e.g., antibodies to pancreatic cells, antibodies to immune cells such as T-cells, monocytes,

dendritic cells, granulocytes, etc., as well as receptor and ligands expressed on pancreatic or immune cells. Other moieties which may be fused to the polypeptide include therapeutic agents which are used for treatment, for example, immunosuppressive drugs such as cyclosporin, SK506, azathioprine, CD3 antibodies and steroids. Also, polypeptides may be fused to immune modulators, and other cytokines such as alpha or beta interferon.

4.6.1 DETERMINING POLYPEPTIDE AND POLYNUCLEOTIDE IDENTITY AND SIMILARITY

Preferred identity and/or similarity are designed to give the largest match between the sequences tested. Methods to determine identity and similarity are codified in computer 10 programs including, but are not limited to, the GCG program package, including GAP (Devereux, J., et al., Nucleic Acids Research 12(1):387 (1984); Genetics Computer Group, University of Wisconsin, Madison, WI), BLASTP, BLASTN, BLASTX, FASTA (Altschul, S.F. et al., J. Molec. Biol. 215:403-410 (1990), PSI-BLAST (Altschul S.F. et al., Nucleic Acids Res. vol. 25, pp. 3389-3402, herein incorporated by reference), eMatrix software (Wu 15 et al., J. Comp. Biol., Vol. 6, pp. 219-235 (1999), herein incorporated by reference), eMotif software (Nevill-Manning et al, ISMB-97, Vol. 4, pp. 202-209, herein incorporated by reference), pFam software (Sonnhammer et al., Nucleic Acids Res., Vol. 26(1), pp. 320-322 (1998), herein incorporated by reference), the GeneAtlas software (Molecular Simulations Inc. (MSI), San Diego, CA) (Sanchez and Sali (1998) Proc. Natl. Acad. Sci., 95, 13597-20 13602; Kitson DH et al, (2000) "Remote homology detection using structural modeling - an evaluation" Submitted; Fischer and Eisenberg (1996) Protein Sci. 5, 947-955), Neural Network Signal PV1.1 program (from Center for Biological Sequence Analysis, The Technical University of Denmark), and the Kyte-Doolittle hydrophobocity prediction algorithm (J. Mol Biol, 157, pp. 105-31 (1982), incorporated herein by reference). The 25 BLAST programs are publicly available from the National Center for Biotechnology Information (NCBI) and other sources (BLAST Manual, Altschul, S., et al. NCB NLM NIH Bethesda, MD 20894; Altschul, S., et al., J. Mol. Biol. 215:403-410 (1990).

4.7 CHIMERIC AND FUSION PROTEINS

The invention also provides chimeric or fusion proteins. As used herein, a "chimeric protein" or "fusion protein" comprises a polypeptide of the invention operatively linked to another polypeptide. Within a fusion protein the polypeptide according to the invention can correspond to all or a portion of a protein according to the invention. In one embodiment, a 35

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fusion protein comprises at least one biologically active portion of a protein according to the invention. In another embodiment, a fusion protein comprises at least two biologically active portions of a protein according to the invention. Within the fusion protein, the term "operatively linked" is intended to indicate that the polypeptide according to the invention and the other polypeptide are fused in-frame to each other. The polypeptide can be fused to the N-terminus or C-terminus.

For example, in one embodiment a fusion protein comprises a polypeptide according to the invention operably linked to the extracellular domain of a second protein.

In another embodiment, the fusion protein is a GST-fusion protein in which the polypeptide sequences of the invention are fused to the C-terminus of the GST (i.e., glutathione S-transferase) sequences.

In another embodiment, the fusion protein is an immunoglobulin fusion protein in which the polypeptide sequences according to the invention comprise one or more domains fused to sequences derived from a member of the immunoglobulin protein family. The immunoglobulin fusion proteins of the invention can be incorporated into pharmaceutical compositions and administered to a subject to inhibit an interaction between a ligand and a protein of the invention on the surface of a cell, to thereby suppress signal transduction in vivo. The immunoglobulin fusion proteins can be used to affect the bioavailability of a cognate ligand. Inhibition of the ligand/protein interaction may be useful therapeutically for both the treatment of proliferative and differentiative disorders, e,g., cancer as well as modulating (e.g., promoting or inhibiting) cell survival. Moreover, the immunoglobulin fusion proteins of the invention can be used as immunogens to produce antibodies in a subject, to purify ligands, and in screening assays to identify molecules that inhibit the interaction of a polypeptide of the invention with a ligand.

A chimeric or fusion protein of the invention can be produced by standard recombinant DNA techniques. For example, DNA fragments coding for the different polypeptide sequences are ligated together in-frame in accordance with conventional techniques, e.g., by employing blunt-ended or stagger-ended termini for ligation, restriction enzyme digestion to provide for appropriate termini, filling-in of cohesive ends as appropriate, alkaline phosphatase treatment to avoid undesirable joining, and enzymatic ligation. In another embodiment, the fusion gene can be synthesized by conventional techniques including automated DNA synthesizers. Alternatively, PCR amplification of gene fragments can be carried out using anchor primers that give rise to complementary overhangs

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between two consecutive gene fragments that can subsequently be annealed and reamplified to generate a chimeric gene sequence (see, for example, Ausubel et al. (eds.) CURRENT PROTOCOLS IN MOLECULAR BIOLOGY, John Wiley & Sons, 1992). Moreover, many expression vectors are commercially available that already encode a fusion moiety (e.g., a GST polypeptide). A nucleic acid encoding a polypeptide of the invention can be cloned into such an expression vector such that the fusion moiety is linked in-frame to the protein of the invention.

4.8 GENE THERAPY

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Mutations in the polynucleotides of the invention may result in loss of normal function of the encoded protein. The invention thus provides gene therapy to restore normal activity of the polypeptides of the invention; or to treat disease states involving polypeptides of the invention. Delivery of a functional gene encoding polypeptides of the invention to appropriate cells is effected ex vivo, in situ, or in vivo by use of vectors, and more particularly viral vectors (e.g., adenovirus, adeno-associated virus, or a retrovirus), or ex vivo by use of physical DNA transfer methods (e.g., liposomes or chemical treatments). See, for example, Anderson, Nature, supplement to vol. 392, no. 6679, pp.25-20 (1998). For additional reviews of gene therapy technology see Friedmann, Science, 244: 1275-1281 (1989); Verma, Scientific American: 68-84 (1990); and Miller, Nature, 357: 455-460 (1992). Introduction of any one of the nucleotides of the present invention or a gene encoding the polypeptides of the present invention can also be accomplished with extrachromosomal substrates (transient expression) or artificial chromosomes (stable expression). Cells may also be cultured ex vivo in the presence of proteins of the present invention in order to proliferate or to produce a desired effect on or activity in such cells. Treated cells can then be introduced in vivo for therapeutic purposes. Alternatively, it is contemplated that in other human disease states, preventing the expression of or inhibiting the activity of polypeptides of the invention will be useful in treating the disease states. It is contemplated that antisense therapy or gene therapy could be applied to negatively regulate the expression of polypeptides of the invention.

Other methods inhibiting expression of a protein include the introduction of antisense molecules to the nucleic acids of the present invention, their complements, or their translated RNA sequences, by methods known in the art. Further, the polypeptides of the present invention can be inhibited by using targeted deletion methods, or the insertion of a negative regulatory element such as a silencer, which is tissue specific.

The present invention still further provides cells genetically engineered in vivo to express the polynucleotides of the invention, wherein such polynucleotides are in operative association with a regulatory sequence heterologous to the host cell which drives expression of the polynucleotides in the cell. These methods can be used to increase or decrease the expression of the polynucleotides of the present invention.

Knowledge of DNA sequences provided by the invention allows for modification of cells to permit, increase, or decrease, expression of endogenous polypeptide. Cells can be modified (e.g., by homologous recombination) to provide increased polypeptide expression by replacing, in whole or in part, the naturally occurring promoter with all or part of a heterologous promoter so that the cells express the protein at higher levels. The heterologous promoter is inserted in such a manner that it is operatively linked to the desired protein encoding sequences. See, for example, PCT International Publication No. WO 94/12650, PCT International Publication No. WO 91/09955. It is also contemplated that, in addition to heterologous promoter DNA, amplifiable marker DNA (e.g., ada, dhfr, and the multifunctional CAD gene which encodes carbamyl phosphate synthase, aspartate transcarbamylase, and dihydroorotase) and/or intron DNA may be inserted along with the heterologous promoter DNA. If linked to the desired protein coding sequence, amplification of the marker DNA by standard selection methods results in co-amplification of the desired protein coding sequences in the cells.

In another embodiment of the present invention, cells and tissues may be engineered to express an endogenous gene comprising the polynucleotides of the invention under the control of inducible regulatory elements, in which case the regulatory sequences of the endogenous gene may be replaced by homologous recombination. As described herein, gene targeting can be used to replace a gene's existing regulatory region with a regulatory sequence isolated from a different gene or a novel regulatory sequence synthesized by genetic engineering methods. Such regulatory sequences may be comprised of promoters, enhancers, scaffold-attachment regions, negative regulatory elements, transcriptional initiation sites, regulatory protein binding sites or combinations of said sequences. Alternatively, sequences which affect the structure or stability of the RNA or protein produced may be replaced, removed, added, or otherwise modified by targeting. These sequences include polyadenylation signals, mRNA stability elements, splice sites, leader sequences for enhancing or modifying transport or secretion properties of the protein, or other sequences which alter or improve the function or stability of protein or RNA molecules.

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The targeting event may be a simple insertion of the regulatory sequence, placing the gene under the control of the new regulatory sequence, e.g., inserting a new promoter or enhancer or both upstream of a gene. Alternatively, the targeting event may be a simple deletion of a regulatory element, such as the deletion of a tissue-specific negative regulatory element. Alternatively, the targeting event may replace an existing element; for example, a tissue-specific enhancer can be replaced by an enhancer that has broader or different cell-type specificity than the naturally occurring elements. Here, the naturally occurring sequences are deleted and new sequences are added. In all cases, the identification of the targeting event may be facilitated by the use of one or more selectable marker genes that are contiguous with the targeting DNA, allowing for the selection of cells in which the exogenous DNA has integrated into the cell genome. The identification of the targeting event may also be facilitated by the use of one or more marker genes exhibiting the property of negative selection, such that the negatively selectable marker is linked to the exogenous DNA, but configured such that the negatively selectable marker flanks the targeting sequence, and such that a correct homologous recombination event with sequences in the host cell genome does not result in the stable integration of the negatively selectable marker. Markers useful for this purpose include the Herpes Simplex Virus thymidine kinase (TK) gene or the bacterial xanthine-guanine phosphoribosyl-transferase (gpt) gene.

The gene targeting or gene activation techniques which can be used in accordance with this aspect of the invention are more particularly described in U.S. Patent No. 5,272,071 to Chappel; U.S. Patent No. 5,578,461 to Sherwin et al.; International Application No. PCT/US92/09627 (WO93/09222) by Selden et al.; and International Application No. PCT/US90/06436 (WO91/06667) by Skoultchi et al., each of which is incorporated by reference herein in its entirety.

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4.9 TRANSGENIC ANIMALS

In preferred methods to determine biological functions of the polypeptides of the invention in vivo, one or more genes provided by the invention are either over expressed or inactivated in the germ line of animals using homologous recombination [Capecchi, Science 244:1288-1292 (1989)]. Animals in which the gene is over expressed, under the regulatory control of exogenous or endogenous promoter elements, are known as transgenic animals. Animals in which an endogenous gene has been inactivated by homologous recombination are referred to as "knockout" animals. Knockout animals, preferably non-human mammals,

can be prepared as described in U.S. Patent No. 5,557,032, incorporated herein by reference. Transgenic animals are useful to determine the roles polypeptides of the invention play in biological processes, and preferably in disease states. Transgenic animals are useful as model systems to identify compounds that modulate lipid metabolism. Transgenic animals, preferably non-human mammals, are produced using methods as described in U.S. Patent No 5,489,743 and PCT Publication No. WO94/28122, incorporated herein by reference.

Transgenic animals can be prepared wherein all or part of a promoter of the polynucleotides of the invention is either activated or inactivated to alter the level of expression of the polypeptides of the invention. Inactivation can be carried out using homologous recombination methods described above. Activation can be achieved by supplementing or even replacing the homologous promoter to provide for increased protein expression. The homologous promoter can be supplemented by insertion of one or more heterologous enhancer elements known to confer promoter activation in a particular tissue.

The polynucleotides of the present invention also make possible the development, through, e.g., homologous recombination or knock out strategies, of animals that fail to express polypeptides of the invention or that express a variant polypeptide. Such animals are useful as models for studying the *in vivo* activities of polypeptide as well as for studying modulators of the polypeptides of the invention.

In preferred methods to determine biological functions of the polypeptides of the invention in vivo, one or more genes provided by the invention are either over expressed or inactivated in the germ line of animals using homologous recombination [Capecchi, Science 244:1288-1292 (1989)]. Animals in which the gene is over expressed, under the regulatory control of exogenous or endogenous promoter elements, are known as transgenic animals. Animals in which an endogenous gene has been inactivated by homologous recombination are referred to as "knockout" animals. Knockout animals, preferably non-human mammals, can be prepared as described in U.S. Patent No. 5,557,032, incorporated herein by reference. Transgenic animals are useful to determine the roles polypeptides of the invention play in biological processes, and preferably in disease states. Transgenic animals are useful as model systems to identify compounds that modulate lipid metabolism. Transgenic animals, preferably non-human mammals, are produced using methods as described in U.S. Patent No 5,489,743 and PCT Publication No. WO94/28122, incorporated herein by reference.

Transgenic animals can be prepared wherein all or part of the polynucleotides of the invention promoter is either activated or inactivated to alter the level of expression of the

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polypeptides of the invention. Inactivation can be carried out using homologous recombination methods described above. Activation can be achieved by supplementing or even replacing the homologous promoter to provide for increased protein expression. The homologous promoter can be supplemented by insertion of one or more heterologous enhancer elements known to confer promoter activation in a particular tissue.

4.10 USES AND BIOLOGICAL ACTIVITY

The polynucleotides and proteins of the present invention are expected to exhibit one or more of the uses or biological activities (including those associated with assays cited herein) identified herein. Uses or activities described for proteins of the present invention may be provided by administration or use of such proteins or of polynucleotides encoding such proteins (such as, for example, in gene therapies or vectors suitable for introduction of DNA). The mechanism underlying the particular condition or pathology will dictate whether the polypeptides of the invention, the polynucleotides of the invention or modulators (activators or inhibitors) thereof would be beneficial to the subject in need of treatment. Thus, "therapeutic compositions of the invention" include compositions comprising isolated polynucleotides (including recombinant DNA molecules, cloned genes and degenerate variants thereof) or polypeptides of the invention (including full length protein, mature protein and truncations or domains thereof), or compounds and other substances that modulate the overall activity of the target gene products, either at the level of target gene/protein expression or target protein activity. Such modulators include polypeptides, analogs, (variants), including fragments and fusion proteins, antibodies and other binding proteins; chemical compounds that directly or indirectly activate or inhibit the polypeptides of the invention (identified, e.g., via drug screening assays as described herein); antisense polynucleotides and polynucleotides suitable for triple helix formation; and in particular antibodies or other binding partners that specifically recognize one or more epitopes of the polypeptides of the invention.

The polypeptides of the present invention may likewise be involved in cellular activation or in one of the other physiological pathways described herein.

4.10.1 RESEARCH USES AND UTILITIES

The polynucleotides provided by the present invention can be used by the research community for various purposes. The polynucleotides can be used to express recombinant

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protein for analysis, characterization or therapeutic use; as markers for tissues in which the corresponding protein is preferentially expressed (either constitutively or at a particular stage of tissue differentiation or development or in disease states); as molecular weight markers on gels; as chromosome markers or tags (when labeled) to identify chromosomes or to map related gene positions; to compare with endogenous DNA sequences in patients to identify potential genetic disorders; as probes to hybridize and thus discover novel, related DNA sequences; as a source of information to derive PCR primers for genetic fingerprinting; as a probe to "subtract-out" known sequences in the process of discovering other novel polynucleotides; for selecting and making oligomers for attachment to a "gene chip" or other support, including for examination of expression patterns; to raise anti-protein antibodies using DNA immunization techniques; and as an antigen to raise anti-DNA antibodies or elicit another immune response. Where the polynucleotide encodes a protein which binds or potentially binds to another protein (such as, for example, in a receptor-ligand interaction), the polynucleotide can also be used in interaction trap assays (such as, for example, that described in Gyuris et al., Cell 75:791-803 (1993)) to identify polynucleotides encoding the other protein with which binding occurs or to identify inhibitors of the binding interaction.

The polypeptides provided by the present invention can similarly be used in assays to determine biological activity, including in a panel of multiple proteins for high-throughput screening; to raise antibodies or to elicit another immune response; as a reagent (including the labeled reagent) in assays designed to quantitatively determine levels of the protein (or its receptor) in biological fluids; as markers for tissues in which the corresponding polypeptide is preferentially expressed (either constitutively or at a particular stage of tissue differentiation or development or in a disease state); and, of course, to isolate correlative receptors or ligands. Proteins involved in these binding interactions can also be used to screen for peptide or small molecule inhibitors or agonists of the binding interaction.

Any or all of these research utilities are capable of being developed into reagent grade or kit format for commercialization as research products.

Methods for performing the uses listed above are well known to those skilled in the art. References disclosing such methods include without limitation "Molecular Cloning: A Laboratory Manual", 2d ed., Cold Spring Harbor Laboratory Press, Sambrook, J., E. F. Fritsch and T. Maniatis eds., 1989, and "Methods in Enzymology: Guide to Molecular Cloning Techniques", Academic Press, Berger, S. L. and A. R. Kimmel eds., 1987.

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4.10.2 NUTRITIONAL USES

Polynucleotides and polypeptides of the present invention can also be used as nutritional sources or supplements. Such uses include without limitation use as a protein or amino acid supplement, use as a carbon source, use as a nitrogen source and use as a source of carbohydrate.

In such cases the polypeptide or polynucleotide of the invention can be added to the feed of a particular organism or can be administered as a separate solid or liquid preparation, such as in the form of powder, pills, solutions, suspensions or capsules. In the case of microorganisms, the polypeptide or polynucleotide of the invention can be added to the medium in or on which the microorganism is cultured.

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4.10.3 CYTOKINE AND CELL PROLIFERATION/DIFFERENTIATION ACTIVITY

A polypeptide of the present invention may exhibit activity relating to cytokine, cell proliferation (either inducing or inhibiting) or cell differentiation (either inducing or inhibiting) activity or may induce production of other cytokines in certain cell populations. A polynucleotide of the invention can encode a polypeptide exhibiting such attributes. Many protein factors discovered to date, including all known cytokines, have exhibited activity in one or more factor-dependent cell proliferation assays, and hence the assays serve as a convenient confirmation of cytokine activity. The activity of therapeutic compositions of the present invention is evidenced by any one of a number of routine factor dependent cell proliferation assays for cell lines including, without limitation, 32D, DA2, DA1G, T10, B9, B9/11, BaF3, MC9/G, M+(preB M+), 2E8, RB5, DA1, 123, T1165, HT2, CTLL2, TF-1, Mo7e, CMK, HUVEC, and Caco. Therapeutic compositions of the invention can be used in the following:

Assays for T-cell or thymocyte proliferation include without limitation those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A. M. Kruisbeek, D. H. Margulies, E. M. Shevach, W. Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, *In Vitro* assays for Mouse Lymphocyte Function 3.1-3.19; Chapter 7, Immunologic studies in Humans); Takai et al., J. Immunol. 137:3494-3500, 1986; Bertagnolli et al., J. Immunol. 145:1706-1712, 1990; Bertagnolli et al., Cellular Immunology 133:327-341, 1991; Bertagnolli, et al., I. Immunol. 149:3778-3783, 1992; Bowman et al., I. Immunol. 152:1756-1761, 1994.

Assays for cytokine production and/or proliferation of spleen cells, lymph node cells or thymocytes include, without limitation, those described in: Polyclonal T cell stimulation, Kruisbeek, A. M. and Shevach, E. M. In Current Protocols in Immunology. J. E. e.a. Coligan eds. Vol 1 pp. 3.12.1-3.12.14, John Wiley and Sons, Toronto. 1994; and Measurement of mouse and human interleukin-γ, Schreiber, R. D. In Current Protocols in Immunology. J. E. e.a. Coligan eds. Vol 1 pp. 6.8.1-6.8.8, John Wiley and Sons, Toronto. 1994.

Assays for proliferation and differentiation of hematopoietic and lymphopoietic cells include, without limitation, those described in: Measurement of Human and Murine Interleukin 2 and Interleukin 4, Bottomly, K., Davis, L. S. and Lipsky, P. E. In Current 10 Protocols in Immunology. J. E. e.a. Coligan eds. Vol 1 pp. 6.3.1-6.3.12, John Wiley and Sons, Toronto. 1991; deVries et al., J. Exp. Med. 173:1205-1211, 1991; Moreau et al., Nature 336:690-692, 1988; Greenberger et al., Proc. Natl. Acad. Sci. U.S.A. 80:2931-2938, 1983; Measurement of mouse and human interleukin 6--Nordan, R. In Current Protocols in Immunology. J. E. Coligan eds. Vol 1 pp. 6.6.1-6.6.5, John Wiley and Sons, Toronto. 1991; 15 Smith et al., Proc. Natl. Aced. Sci. U.S.A. 83:1857-1861, 1986; Measurement of human Interleukin 11--Bennett, F., Giannotti, J., Clark, S. C. and Turner, K. J. In Current Protocols in Immunology. J. E. Coligan eds. Vol 1 pp. 6.15.1 John Wiley and Sons, Toronto. 1991; Measurement of mouse and human Interleukin 9-Ciarletta, A., Giannotti, J., Clark, S. C. and Turner, K. J. In Current Protocols in Immunology, J. E. Coligan eds. Vol 1 pp. 6.13.1, John 20 Wiley and Sons, Toronto. 1991.

Assays for T-cell clone responses to antigens (which will identify, among others, proteins that affect APC-T cell interactions as well as direct T-cell effects by measuring proliferation and cytokine production) include, without limitation, those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A. M. Kruisbeek, D. H. Margulies, E. M. Shevach, W Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, *In Vitro* assays for Mouse Lymphocyte Function; Chapter 6, Cytokines and their cellular receptors; Chapter 7, Immunologic studies in Humans); Weinberger et al., Proc. Natl. Acad. Sci. USA 77:6091-6095, 1980; Weinberger et al., Eur. J. Immunol. 11:405-411, 1981; Takai et al., J. Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988.

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4.10.4 STEM CELL GROWTH FACTOR ACTIVITY

A polypeptide of the present invention may exhibit stem cell growth factor activity and be involved in the proliferation, differentiation and survival of pluripotent and totipotent

stem cells including primordial germ cells, embryonic stem cells, hematopoietic stem cells and/or germ line stem cells. Administration of the polypeptide of the invention to stem cells in vivo or ex vivo is expected to maintain and expand cell populations in a totipotential or pluripotential state which would be useful for re-engineering damaged or diseased tissues, transplantation, manufacture of bio-pharmaceuticals and the development of bio-sensors. The ability to produce large quantities of human cells has important working applications for the production of human proteins which currently must be obtained from non-human sources or donors, implantation of cells to treat diseases such as Parkinson's, Alzheimer's and other neurodegenerative diseases; tissues for grafting such as bone marrow, skin, cartilage, tendons, bone, muscle (including cardiac muscle), blood vessels, cornea, neural cells, gastrointestinal cells and others; and organs for transplantation such as kidney, liver, pancreas (including islet cells), heart and lung.

It is contemplated that multiple different exogenous growth factors and/or cytokines may be administered in combination with the polypeptide of the invention to achieve the desired effect, including any of the growth factors listed herein, other stem cell maintenance factors, and specifically including stem cell factor (SCF), leukemia inhibitory factor (LIF), Flt-3 ligand (Flt-3L), any of the interleukins, recombinant soluble IL-6 receptor fused to IL-6, macrophage inflammatory protein 1-alpha (MIP-1-alpha), G-CSF, GM-CSF, thrombopoietin (TPO), platelet factor 4 (PF-4), platelet-derived growth factor (PDGF), neural growth factors and basic fibroblast growth factor (bFGF).

Since totipotent stem cells can give rise to virtually any mature cell type, expansion of these cells in culture will facilitate the production of large quantities of mature cells. Techniques for culturing stem cells are known in the art and administration of polypeptides of the invention, optionally with other growth factors and/or cytokines, is expected to enhance the survival and proliferation of the stem cell populations. This can be accomplished by direct administration of the polypeptide of the invention to the culture medium.

Alternatively, stroma cells transfected with a polynucleotide that encodes for the polypeptide of the invention can be used as a feeder layer for the stem cell populations in culture or in vivo. Stromal support cells for feeder layers may include embryonic bone marrow fibroblasts, bone marrow stromal cells, fetal liver cells, or cultured embryonic fibroblasts (see U.S. Patent No. 5,690,926).

Stem cells themselves can be transfected with a polynucleotide of the invention to induce autocrine expression of the polypeptide of the invention. This will allow for

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generation of undifferentiated totipotential/pluripotential stem cell lines that are useful as is or that can then be differentiated into the desired mature cell types. These stable cell lines can also serve as a source of undifferentiated totipotential/pluripotential mRNA to create cDNA libraries and templates for polymerase chain reaction experiments. These studies would allow for the isolation and identification of differentially expressed genes in stem cell populations that regulate stem cell proliferation and/or maintenance.

Expansion and maintenance of totipotent stem cell populations will be useful in the treatment of many pathological conditions. For example, polypeptides of the present invention may be used to manipulate stem cells in culture to give rise to neuroepithelial cells that can be used to augment or replace cells damaged by illness, autoimmune disease, accidental damage or genetic disorders. The polypeptide of the invention may be useful for inducing the proliferation of neural cells and for the regeneration of nerve and brain tissue, i.e. for the treatment of central and peripheral nervous system diseases and neuropathies, as well as mechanical and traumatic disorders which involve degeneration, death or trauma to neural cells or nerve tissue. In addition, the expanded stem cell populations can also be genetically altered for gene therapy purposes and to decrease host rejection of replacement tissues after grafting or implantation.

Expression of the polypeptide of the invention and its effect on stem cells can also be manipulated to achieve controlled differentiation of the stem cells into more differentiated cell types. A broadly applicable method of obtaining pure populations of a specific differentiated cell type from undifferentiated stem cell populations involves the use of a cell-type specific promoter driving a selectable marker. The selectable marker allows only cells of the desired type to survive. For example, stem cells can be induced to differentiate into cardiomyocytes (Wobus et al., Differentiation, 48: 173-182, (1991); Klug et al., J. Clin. Invest., 98(1): 216-224, (1998)) or skeletal muscle cells (Browder, L. W. In: *Principles of Tissue Engineering eds.* Lanza et al., Academic Press (1997)). Alternatively, directed differentiation of stem cells can be accomplished by culturing the stem cells in the presence of a differentiation factor such as retinoic acid and an antagonist of the polypeptide of the invention which would inhibit the effects of endogenous stem cell factor activity and allow differentiation to proceed.

In vitro cultures of stem cells can be used to determine if the polypeptide of the invention exhibits stem cell growth factor activity. Stem cells are isolated from any one of various cell sources (including hematopoietic stem cells and embryonic stem cells) and

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cultured on a feeder layer, as described by Thompson et al. Proc. Natl. Acad. Sci, U.S.A., 92: 7844-7848 (1995), in the presence of the polypeptide of the invention alone or in combination with other growth factors or cytokines. The ability of the polypeptide of the invention to induce stem cells proliferation is determined by colony formation on semi-solid support e.g. as described by Bernstein et al., Blood, 77: 2316-2321 (1991).

4.10.5 HEMATOPOIESIS REGULATING ACTIVITY

A polypeptide of the present invention may be involved in regulation of hematopoiesis and, consequently, in the treatment of myeloid or lymphoid cell disorders. Even marginal biological activity in support of colony forming cells or of factor-dependent cell lines indicates involvement in regulating hematopoiesis, e.g. in supporting the growth and proliferation of erythroid progenitor cells alone or in combination with other cytokines, thereby indicating utility, for example, in treating various anemias or for use in conjunction with irradiation/chemotherapy to stimulate the production of erythroid precursors and/or erythroid cells; in supporting the growth and proliferation of myeloid cells such as granulocytes and monocytes/macrophages (i.e., traditional CSF activity) useful, for example, in conjunction with chemotherapy to prevent or treat consequent myelo-suppression; in supporting the growth and proliferation of megakaryocytes and consequently of platelets thereby allowing prevention or treatment of various platelet disorders such as thrombocytopenia, and generally for use in place of or complimentary to platelet transfusions; and/or in supporting the growth and proliferation of hematopoietic stem cells which are capable of maturing to any and all of the above-mentioned hematopoietic cells and therefore find therapeutic utility in various stem cell disorders (such as those usually treated with transplantation, including, without limitation, aplastic anemia and paroxysmal nocturnal hemoglobinuria), as well as in repopulating the stem cell compartment post irradiation/chemotherapy, either in-vivo or ex-vivo (i.e., in conjunction with bone marrow transplantation or with peripheral progenitor cell transplantation (homologous or heterologous)) as normal cells or genetically manipulated for gene therapy.

Therapeutic compositions of the invention can be used in the following:

Suitable assays for proliferation and differentiation of various hematopoietic lines are cited above.

Assays for embryonic stem cell differentiation (which will identify, among others, proteins that influence embryonic differentiation hematopoiesis) include, without limitation,

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those described in: Johansson et al. Cellular Biology 15:141-151, 1995; Keller et al., Molecular and Cellular Biology 13:473-486, 1993; McClanahan et al., Blood 81:2903-2915, 1993.

Assays for stem cell survival and differentiation (which will identify, among others, 5 proteins that regulate lympho-hematopoiesis) include, without limitation, those described in: Methylcellulose colony forming assays, Freshney, M. G. In Culture of Hematopoietic Cells. R. I. Freshney, et al. eds. Vol pp. 265-268, Wiley-Liss, Inc., New York, N.Y. 1994; Hirayama et al., Proc. Natl. Acad. Sci. USA 89:5907-5911, 1992; Primitive hematopoietic colony forming cells with high proliferative potential, McNiece, I. K. and Briddell, R. A. In Culture 10 of Hematopoietic Cells. R. I. Freshney, et al. eds. Vol pp. 23-39, Wiley-Liss, Inc., New York, N.Y. 1994; Neben et al., Experimental Hematology 22:353-359, 1994; Cobblestone area forming cell assay, Ploemacher, R. E. In Culture of Hematopoietic Cells. R. I. Freshney, et al. eds. Vol pp. 1-21, Wiley-Liss, Inc., New York, N.Y. 1994; Long term bone marrow cultures in the presence of stromal cells, Spooncer, E., Dexter, M. and Allen, T. In Culture of Hematopoietic Cells. R. I. Freshney, et al. eds. Vol pp. 163-179, Wiley-Liss, Inc., New York, N.Y. 1994; Long term culture initiating cell assay, Sutherland, H. J. In Culture of Hematopoietic Cells. R. I. Freshney, et al. eds. Vol pp. 139-162, Wiley-Liss, Inc., New York, N.Y. 1994.

4.10.6 TISSUE GROWTH ACTIVITY

A polypeptide of the present invention also may be involved in bone, cartilage, tendon, ligament and/or nerve tissue growth or regeneration, as well as in wound healing and tissue repair and replacement, and in healing of burns, incisions and ulcers.

A polypeptide of the present invention which induces cartilage and/or bone growth in circumstances where bone is not normally formed, has application in the healing of bone fractures and cartilage damage or defects in humans and other animals. Compositions of a polypeptide, antibody, binding partner, or other modulator of the invention may have prophylactic use in closed as well as open fracture reduction and also in the improved fixation of artificial joints. De novo bone formation induced by an osteogenic agent contributes to the repair of congenital, trauma induced, or oncologic resection induced craniofacial defects, and also is useful in cosmetic plastic surgery.

A polypeptide of this invention may also be involved in attracting bone-forming cells, stimulating growth of bone-forming cells, or inducing differentiation of progenitors of

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bone-forming cells. Treatment of osteoporosis, osteoarthritis, bone degenerative disorders, or periodontal disease, such as through stimulation of bone and/or cartilage repair or by blocking inflammation or processes of tissue destruction (collagenase activity, osteoclast activity, etc.) mediated by inflammatory processes may also be possible using the composition of the invention.

Another category of tissue regeneration activity that may involve the polypeptide of the present invention is tendon/ligament formation. Induction of tendon/ligament-like tissue or other tissue formation in circumstances where such tissue is not normally formed, has application in the healing of tendon or ligament tears, deformities and other tendon or ligament defects in humans and other animals. Such a preparation employing a tendon/ligament-like tissue inducing protein may have prophylactic use in preventing damage to tendon or ligament tissue, as well as use in the improved fixation of tendon or ligament to bone or other tissues, and in repairing defects to tendon or ligament tissue. De novo tendon/ligament-like tissue formation induced by a composition of the present invention contributes to the repair of congenital, trauma induced, or other tendon or ligament defects of other origin, and is also useful in cosmetic plastic surgery for attachment or repair of tendons or ligaments. The compositions of the present invention may provide environment to attract tendon- or ligament-forming cells, stimulate growth of tendon- or ligament-forming cells, induce differentiation of progenitors of tendon- or ligament-forming cells, or induce growth of tendon/ligament cells or progenitors ex vivo for return in vivo to effect tissue repair. The compositions of the invention may also be useful in the treatment of tendinitis, carpal tunnel syndrome and other tendon or ligament defects. The compositions may also include an appropriate matrix and/or sequestering agent as a carrier as is well known in the art.

The compositions of the present invention may also be useful for proliferation of neural cells and for regeneration of nerve and brain tissue, i.e. for the treatment of central and peripheral nervous system diseases and neuropathies, as well as mechanical and traumatic disorders, which involve degeneration, death or trauma to neural cells or nerve tissue. More specifically, a composition may be used in the treatment of diseases of the peripheral nervous system, such as peripheral nerve injuries, peripheral neuropathy and localized neuropathies, and central nervous system diseases, such as Alzheimer's, Parkinson's disease, Huntington's disease, amyotrophic lateral sclerosis, and Shy-Drager syndrome. Further conditions which may be treated in accordance with the present invention include mechanical and traumatic disorders, such as spinal cord disorders, head trauma and cerebrovascular diseases such as

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stroke. Peripheral neuropathies resulting from chemotherapy or other medical therapies may also be treatable using a composition of the invention.

Compositions of the invention may also be useful to promote better or faster closure of non-healing wounds, including without limitation pressure ulcers, ulcers associated with vascular insufficiency, surgical and traumatic wounds, and the like.

Compositions of the present invention may also be involved in the generation or regeneration of other tissues, such as organs (including, for example, pancreas, liver, intestine, kidney, skin, endothelium), muscle (smooth, skeletal or cardiac) and vascular (including vascular endothelium) tissue, or for promoting the growth of cells comprising such tissues. Part of the desired effects may be by inhibition or modulation of fibrotic scarring may allow normal tissue to regenerate. A polypeptide of the present invention may also exhibit angiogenic activity.

A composition of the present invention may also be useful for gut protection or regeneration and treatment of lung or liver fibrosis, reperfusion injury in various tissues, and conditions resulting from systemic cytokine damage.

A composition of the present invention may also be useful for promoting or inhibiting differentiation of tissues described above from precursor tissues or cells; or for inhibiting the growth of tissues described above.

Therapeutic compositions of the invention can be used in the following:

Assays for tissue generation activity include, without limitation, those described in: International Patent Publication No. WO95/16035 (bone, cartilage, tendon); International Patent Publication No. WO95/05846 (nerve, neuronal); International Patent Publication No. WO91/07491 (skin, endothelium).

Assays for wound healing activity include, without limitation, those described in: Winter, Epidermal Wound Healing, pps. 71-112 (Maibach, H. I. and Rovee, D. T., eds.), Year Book Medical Publishers, Inc., Chicago, as modified by Eaglstein and Mertz, J. Invest. Dermatol 71:382-84 (1978).

4.10.7 IMMUNE STIMULATING OR SUPPRESSING ACTIVITY

A polypeptide of the present invention may also exhibit immune stimulating or immune suppressing activity, including without limitation the activities for which assays are described herein. A polynucleotide of the invention can encode a polypeptide exhibiting such activities. A protein may be useful in the treatment of various immune deficiencies and

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disorders (including severe combined immunodeficiency (SCID)), e.g., in regulating (up or down) growth and proliferation of T and/or B lymphocytes, as well as effecting the cytolytic activity of NK cells and other cell populations. These immune deficiencies may be genetic or be caused by viral (e.g., HIV) as well as bacterial or fungal infections, or may result from autoimmune disorders. More specifically, infectious diseases causes by viral, bacterial, fungal or other infection may be treatable using a protein of the present invention, including infections by HIV, hepatitis viruses, herpes viruses, mycobacteria, Leishmania spp., malaria spp. and various fungal infections such as candidiasis. Of course, in this regard, proteins of the present invention may also be useful where a boost to the immune system generally may be desirable, i.e., in the treatment of cancer.

Autoimmune disorders which may be treated using a protein of the present invention include, for example, connective tissue disease, multiple sclerosis, systemic lupus erythematosus, rheumatoid arthritis, autoimmune pulmonary inflammation, Guillain-Barre syndrome, autoimmune thyroiditis, insulin dependent diabetes mellitis, myasthenia gravis, graft-versus-host disease and autoimmune inflammatory eye disease. Such a protein (or antagonists thereof, including antibodies) of the present invention may also to be useful in the treatment of allergic reactions and conditions (e.g., anaphylaxis, serum sickness, drug reactions, food allergies, insect venom allergies, mastocytosis, allergic rhinitis, hypersensitivity pneumonitis, urticaria, angioedema, eczema, atopic dermatitis, allergic contact dermatitis, erythema multiforme, Stevens-Johnson syndrome, allergic conjunctivitis, atopic keratoconjunctivitis, venereal keratoconjunctivitis, giant papillary conjunctivitis and contact allergies), such as asthma (particularly allergic asthma) or other respiratory problems. Other conditions, in which immune suppression is desired (including, for example, organ transplantation), may also be treatable using a protein (or antagonists thereof) of the present invention. The therapeutic effects of the polypeptides or antagonists thereof on allergic reactions can be evaluated by in vivo animals models such as the cumulative contact enhancement test (Lastbom et al., Toxicology 125: 59-66, 1998), skin prick test (Hoffmann et al., Allergy 54: 446-54, 1999), guinea pig skin sensitization test (Vohr et al., Arch. Toxocol. 73: 501-9), and murine local lymph node assay (Kimber et al., J. Toxicol. Environ. Health 53: 563-79).

Using the proteins of the invention it may also be possible to modulate immune responses, in a number of ways. Down regulation may be in the form of inhibiting or blocking an immune response already in progress or may involve preventing the induction of

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an immune response. The functions of activated T cells may be inhibited by suppressing T cell responses or by inducing specific tolerance in T cells, or both. Immunosuppression of T cell responses is generally an active, non-antigen-specific, process which requires continuous exposure of the T cells to the suppressive agent. Tolerance, which involves inducing non-responsiveness or anergy in T cells, is distinguishable from immunosuppression in that it is generally antigen-specific and persists after exposure to the tolerizing agent has ceased. Operationally, tolerance can be demonstrated by the lack of a T cell response upon reexposure to specific antigen in the absence of the tolerizing agent.

Down regulating or preventing one or more antigen functions (including without limitation B lymphocyte antigen functions (such as, for example, B7)), e.g., preventing high level lymphokine synthesis by activated T cells, will be useful in situations of tissue, skin and organ transplantation and in graft-versus-host disease (GVHD). For example, blockage of T cell function should result in reduced tissue destruction in tissue transplantation. Typically, in tissue transplants, rejection of the transplant is initiated through its recognition as foreign by T cells, followed by an immune reaction that destroys the transplant. The administration of a therapeutic composition of the invention may prevent cytokine synthesis by immune cells, such as T cells, and thus acts as an immunosuppressant. Moreover, a lack of costimulation may also be sufficient to anergize the T cells, thereby inducing tolerance in a subject. Induction of long-term tolerance by B lymphocyte antigen-blocking reagents may avoid the necessity of repeated administration of these blocking reagents. To achieve sufficient immunosuppression or tolerance in a subject, it may also be necessary to block the function of a combination of B lymphocyte antigens.

The efficacy of particular therapeutic compositions in preventing organ transplant rejection or GVHD can be assessed using animal models that are predictive of efficacy in humans. Examples of appropriate systems which can be used include allogeneic cardiac grafts in rats and xenogeneic pancreatic islet cell grafts in mice, both of which have been used to examine the immunosuppressive effects of CTLA4Ig fusion proteins in vivo as described in Lenschow et al., Science 257:789-792 (1992) and Turka et al., Proc. Natl. Acad. Sci USA, 89:11102-11105 (1992). In addition, murine models of GVHD (see Paul ed., Fundamental Immunology, Raven Press, New York, 1989, pp. 846-847) can be used to determine the effect of therapeutic compositions of the invention on the development of that disease.

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Blocking antigen function may also be therapeutically useful for treating autoimmune diseases. Many autoimmune disorders are the result of inappropriate activation of T cells that are reactive against self tissue and which promote the production of cytokines and autoantibodies involved in the pathology of the diseases. Preventing the activation of autoreactive T cells may reduce or eliminate disease symptoms. Administration of reagents which block stimulation of T cells can be used to inhibit T cell activation and prevent production of autoantibodies or T cell-derived cytokines which may be involved in the disease process. Additionally, blocking reagents may induce antigen-specific tolerance of autoreactive T cells which could lead to long-term relief from the disease. The efficacy of blocking reagents in preventing or alleviating autoimmune disorders can be determined using a number of well-characterized animal models of human autoimmune diseases. Examples include murine experimental autoimmune encephalitis, systemic lupus erythmatosis in MRL/lpr/lpr mice or NZB hybrid mice, murine autoimmune collagen arthritis, diabetes mellitus in NOD mice and BB rats, and murine experimental myasthenia gravis (see Paul ed., Fundamental Immunology, Raven Press, New York, 1989, pp. 840-856).

Upregulation of an antigen function (e.g., a B lymphocyte antigen function), as a means of up regulating immune responses, may also be useful in therapy. Upregulation of immune responses may be in the form of enhancing an existing immune response or eliciting an initial immune response. For example, enhancing an immune response may be useful in cases of viral infection, including systemic viral diseases such as influenza, the common cold, and encephalitis.

Alternatively, anti-viral immune responses may be enhanced in an infected patient by removing T cells from the patient, costimulating the T cells in vitro with viral antigen-pulsed APCs either expressing a peptide of the present invention or together with a stimulatory form of a soluble peptide of the present invention and reintroducing the in vitro activated T cells into the patient. Another method of enhancing anti-viral immune responses would be to isolate infected cells from a patient, transfect them with a nucleic acid encoding a protein of the present invention as described herein such that the cells express all or a portion of the protein on their surface, and reintroduce the transfected cells into the patient. The infected cells would now be capable of delivering a costimulatory signal to, and thereby activate, T cells in vivo.

A polypeptide of the present invention may provide the necessary stimulation signal to T cells to induce a T cell mediated immune response against the transfected tumor cells. In

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addition, tumor cells which lack MHC class I or MHC class II molecules, or which fail to reexpress sufficient mounts of MHC class I or MHC class II molecules, can be transfected with nucleic acid encoding all or a portion of (e.g., a cytoplasmic-domain truncated portion) of an MHC class I alpha chain protein and β₂ microglobulin protein or an MHC class II alpha chain protein and an MHC class II beta chain protein to thereby express MHC class I or MHC class II proteins on the cell surface. Expression of the appropriate class I or class II MHC in conjunction with a peptide having the activity of a B lymphocyte antigen (e.g., B7-1, B7-2, B7-3) induces a T cell mediated immune response against the transfected tumor cell. Optionally, a gene encoding an antisense construct which blocks expression of an MHC class II associated protein, such as the invariant chain, can also be cotransfected with a DNA encoding a peptide having the activity of a B lymphocyte antigen to promote presentation of tumor associated antigens and induce tumor specific immunity. Thus, the induction of a T cell mediated immune response in a human subject may be sufficient to overcome tumor-specific tolerance in the subject.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Suitable assays for thymocyte or splenocyte cytotoxicity include, without limitation, those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A. M. Kruisbeek, D. H. Margulies, E. M. Shevach, W. Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse Lymphocyte Function 3.1-3.19; Chapter 7, Immunologic studies in Humans); Herrmann et al., Proc. Natl. Acad. Sci. USA 78:2488-2492, 1981; Herrmann et al., J. Immunol. 128:1968-1974, 1982; Handa et al., J. Immunol. 135:1564-1572, 1985; Takai et al., I. Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988; Bowman et al., J. Virology 61:1992-1998; Bertagnolli et al., Cellular Immunology 133:327-341, 1991; Brown et al., J. Immunol. 153:3079-3092, 1994.

Assays for T-cell-dependent immunoglobulin responses and isotype switching (which will identify, among others, proteins that modulate T-cell dependent antibody responses and that affect Th1/Th2 profiles) include, without limitation, those described in: Maliszewski, J. Immunol. 144:3028-3033, 1990; and Assays for B cell function: In vitro antibody production, Mond, J. J. and Brunswick, M. In Current Protocols in Immunology. J. E. e.a. Coligan eds. Vol 1 pp. 3.8.1-3.8.16, John Wiley and Sons, Toronto. 1994.

Mixed lymphocyte reaction (MLR) assays (which will identify, among others, proteins that generate predominantly Th1 and CTL responses) include, without limitation,

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those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A. M. Kruisbeek, D. H. Margulies, E. M. Shevach, W. Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse Lymphocyte Function 3.1-3.19; Chapter 7, Immunologic studies in Humans); Takai et al., J. Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988; Bertagnolli et al., J. Immunol. 149:3778-3783, 1992.

Dendritic cell-dependent assays (which will identify, among others, proteins expressed by dendritic cells that activate naive T-cells) include, without limitation, those described in: Guery et al., J. Immunol. 134:536-544, 1995; Inaba et al., Journal of Experimental Medicine 173:549-559, 1991; Macatonia et al., Journal of Immunology 154:5071-5079, 1995; Porgador et al., Journal of Experimental Medicine 182:255-260, 1995; Nair et al., Journal of Virology 67:4062-4069, 1993; Huang et al., Science 264:961-965, 1994; Macatonia et al., Journal of Experimental Medicine 169:1255-1264, 1989; Bhardwaj et al., Journal of Clinical Investigation 94:797-807, 1994; and Inaba et al., Journal of Experimental Medicine 172:631-640, 1990.

Assays for lymphocyte survival/apoptosis (which will identify, among others, proteins that prevent apoptosis after superantigen induction and proteins that regulate lymphocyte homeostasis) include, without limitation, those described in: Darzynkiewicz et al., Cytometry 13:795-808, 1992; Gorczyca et al., Leukemia 7:659-670, 1993; Gorczyca et al., Cancer Research 53:1945-1951, 1993; Itoh et al., Cell 66:233-243, 1991; Zacharchuk, Journal of Immunology 145:4037-4045, 1990; Zamai et al., Cytometry 14:891-897, 1993; Gorczyca et al., International Journal of Oncology 1:639-648, 1992.

Assays for proteins that influence early steps of T-cell commitment and development include, without limitation, those described in: Antica et al., Blood 84:111-117, 1994; Fine et al., Cellular Immunology 155:111-122, 1994; Galy et al., Blood 85:2770-2778, 1995; Toki et al., Proc. Nat. Acad Sci. USA 88:7548-7551, 1991.

4.10.8 ACTIVIN/INHIBIN ACTIVITY

A polypeptide of the present invention may also exhibit activin- or inhibin-related activities. A polynucleotide of the invention may encode a polypeptide exhibiting such characteristics. Inhibins are characterized by their ability to inhibit the release of follicle stimulating hormone (FSH), while activins and are characterized by their ability to stimulate the release of follicle stimulating hormone (FSH). Thus, a polypeptide of the present

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invention, alone or in heterodimers with a member of the inhibin family, may be useful as a contraceptive based on the ability of inhibins to decrease fertility in female mammals and decrease spermatogenesis in male mammals. Administration of sufficient amounts of other inhibins can induce infertility in these mammals. Alternatively, the polypeptide of the invention, as a homodimer or as a heterodimer with other protein subunits of the inhibin group, may be useful as a fertility inducing therapeutic, based upon the ability of activin molecules in stimulating FSH release from cells of the anterior pituitary. See, for example, U.S. Pat. No. 4,798,885. A polypeptide of the invention may also be useful for advancement of the onset of fertility in sexually immature mammals, so as to increase the lifetime reproductive performance of domestic animals such as, but not limited to, cows, sheep and pigs.

The activity of a polypeptide of the invention may, among other means, be measured by the following methods.

Assays for activin/inhibin activity include, without limitation, those described in: Vale et al., Endocrinology 91:562-572, 1972; Ling et al., Nature 321:779-782, 1986; Vale et al., Nature 321:776-779, 1986; Mason et al., Nature 318:659-663, 1985; Forage et al., Proc. Natl. Acad. Sci. USA 83:3091-3095, 1986.

4.10.9 CHEMOTACTIC/CHEMOKINETIC ACTIVITY

A polypeptide of the present invention may be involved in chemotactic or chemokinetic activity for mammalian cells, including, for example, monocytes, fibroblasts, neutrophils, T-cells, mast cells, eosinophils, epithelial and/or endothelial cells. A polynucleotide of the invention can encode a polypeptide exhibiting such attributes. Chemotactic and chemokinetic receptor activation can be used to mobilize or attract a desired cell population to a desired site of action. Chemotactic or chemokinetic compositions (e.g. proteins, antibodies, binding partners, or modulators of the invention) provide particular advantages in treatment of wounds and other trauma to tissues, as well as in treatment of localized infections. For example, attraction of lymphocytes, monocytes or neutrophils to tumors or sites of infection may result in improved immune responses against the tumor or infecting agent.

A protein or peptide has chemotactic activity for a particular cell population if it can stimulate, directly or indirectly, the directed orientation or movement of such cell population. Preferably, the protein or peptide has the ability to directly stimulate directed movement of

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cells. Whether a particular protein has chemotactic activity for a population of cells can be readily determined by employing such protein or peptide in any known assay for cell chemotaxis.

Therapeutic compositions of the invention can be used in the following:

Assays for chemotactic activity (which will identify proteins that induce or prevent chemotaxis) consist of assays that measure the ability of a protein to induce the migration of cells across a membrane as well as the ability of a protein to induce the adhesion of one cell population to another cell population. Suitable assays for movement and adhesion include, without limitation, those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A. M. Kruisbeek, D. H. Marguiles, E. M. Shevach, W. Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 6.12, Measurement of alpha and beta Chemokines 6.12.1-6.12.28; Taub et al. J. Clin. Invest. 95:1370-1376, 1995; Lind et al. APMIS 103:140-146, 1995; Muller et al Eur. J. Immunol. 25:1744-1748; Gruber et al. J. of Immunol. 152:5860-5867, 1994; Johnston et al. J. of Immunol. 153:1762-1768, 1994.

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4.10.10 HEMOSTATIC AND THROMBOLYTIC ACTIVITY

A polypeptide of the invention may also be involved in hemostasis or thrombolysis or thrombosis. A polynucleotide of the invention can encode a polypeptide exhibiting such attributes. Compositions may be useful in treatment of various coagulation disorders (including hereditary disorders, such as hemophilias) or to enhance coagulation and other hemostatic events in treating wounds resulting from trauma, surgery or other causes. A composition of the invention may also be useful for dissolving or inhibiting formation of thromboses and for treatment and prevention of conditions resulting therefrom (such as, for example, infarction of cardiac and central nervous system vessels (e.g., stroke).

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Therapeutic compositions of the invention can be used in the following:

Assay for hemostatic and thrombolytic activity include, without limitation, those described in: Linet et al., J. Clin. Pharmacol. 26:131-140, 1986; Burdick et al., Thrombosis Res. 45:413-419, 1987; Humphrey et al., Fibrinolysis 5:71-79 (1991); Schaub, Prostaglandins 35:467-474, 1988.

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4.10.11 CANCER DIAGNOSIS AND THERAPY

Polypeptides of the invention may be involved in cancer cell generation, proliferation or metastasis. Detection of the presence or amount of polynucleotides or polypeptides of the

invention may be useful for the diagnosis and/or prognosis of one or more types of cancer. For example, the presence or increased expression of a polynucleotide/polypeptide of the invention may indicate a hereditary risk of cancer, a precancerous condition, or an ongoing malignancy. Conversely, a defect in the gene or absence of the polypeptide may be associated with a cancer condition. Identification of single nucleotide polymorphisms associated with cancer or a predisposition to cancer may also be useful for diagnosis or prognosis.

Cancer treatments promote tumor regression by inhibiting tumor cell proliferation, inhibiting angiogenesis (growth of new blood vessels that is necessary to support tumor growth) and/or prohibiting metastasis by reducing tumor cell motility or invasiveness. Therapeutic compositions of the invention may be effective in adult and pediatric oncology including in solid phase tumors/malignancies, locally advanced tumors, human soft tissue sarcomas, metastatic cancer, including lymphatic metastases, blood cell malignancies including multiple myeloma, acute and chronic leukemias, and lymphomas, head and neck cancers including mouth cancer, larynx cancer and thyroid cancer, lung cancers including small cell carcinoma and non-small cell cancers, breast cancers including small cell carcinoma and ductal carcinoma, gastrointestinal cancers including esophageal cancer, stomach cancer, colon cancer, colorectal cancer and polyps associated with colorectal neoplasia, pancreatic cancers, liver cancer, urologic cancers including bladder cancer and prostate cancer, malignancies of the female genital tract including ovarian carcinoma, uterine (including endometrial) cancers, and solid tumor in the ovarian follicle, kidney cancers including renal cell carcinoma, brain cancers including intrinsic brain tumors, neuroblastoma, astrocytic brain tumors, gliomas, metastatic tumor cell invasion in the central nervous system, bone cancers including osteomas, skin cancers including malignant melanoma, tumor progression of human skin keratinocytes, squamous cell carcinoma, basal cell carcinoma, hemangiopericytoma and Karposi's sarcoma.

Polypeptides, polynucleotides, or modulators of polypeptides of the invention (including inhibitors and stimulators of the biological activity of the polypeptide of the invention) may be administered to treat cancer. Therapeutic compositions can be administered in therapeutically effective dosages alone or in combination with adjuvant cancer therapy such as surgery, chemotherapy, radiotherapy, thermotherapy, and laser therapy, and may provide a beneficial effect, e.g. reducing tumor size, slowing rate of tumor growth, inhibiting metastasis, or otherwise improving overall clinical condition, without

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necessarily eradicating the cancer.

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The composition can also be administered in therapeutically effective amounts as a portion of an anti-cancer cocktail. An anti-cancer cocktail is a mixture of the polypeptide or modulator of the invention with one or more anti-cancer drugs in addition to a pharmaceutically acceptable carrier for delivery. The use of anti-cancer cocktails as a cancer treatment is routine. Anti-cancer drugs that are well known in the art and can be used as a treatment in combination with the polypeptide or modulator of the invention include: Actinomycin D, Aminoglutethimide, Asparaginase, Bleomycin, Busulfan, Carboplatin, Carmustine, Chlorambucil, Cisplatin (cis-DDP), Cyclophosphamide, Cytarabine HCl (Cytosine arabinoside), Dacarbazine, Dactinomycin, Daunorubicin HCl, Doxorubicin HCl, Estramustine phosphate sodium, Etoposide (V16-213), Floxuridine, 5-Fluorouracil (5-Fu), Flutamide, Hydroxyurea (hydroxycarbamide), Ifosfamide, Interferon Alpha-2a, Interferon Alpha-2b, Leuprolide acetate (LHRH-releasing factor analog), Lomustine, Mechlorethamine HCl (nitrogen mustard), Melphalan, Mercaptopurine, Mesna, Methotrexate (MTX), Mitomycin, Mitoxantrone HCl, Octreotide, Plicamycin, Procarbazine HCl, Streptozocin, Tamoxifen citrate, Thioguanine, Thiotepa, Vinblastine sulfate, Vincristine sulfate, Amsacrine, Azacitidine, Hexamethylmelamine, Interleukin-2, Mitoguazone, Pentostatin, Semustine, Teniposide, and Vindesine sulfate.

In addition, therapeutic compositions of the invention may be used for prophylactic treatment of cancer. There are hereditary conditions and/or environmental situations (e.g. exposure to carcinogens) known in the art that predispose an individual to developing cancers. Under these circumstances, it may be beneficial to treat these individuals with therapeutically effective doses of the polypeptide of the invention to reduce the risk of developing cancers.

In vitro models can be used to determine the effective doses of the polypeptide of the invention as a potential cancer treatment. These in vitro models include proliferation assays of cultured tumor cells, growth of cultured tumor cells in soft agar (see Freshney, (1987) Culture of Animal Cells: A Manual of Basic Technique, Wily-Liss, New York, NY Ch 18 and Ch 21), tumor systems in nude mice as described in Giovanella et al., J. Natl. Can. Inst., 52: 921-30 (1974), mobility and invasive potential of tumor cells in Boyden Chamber assays as described in Pilkington et al., Anticancer Res., 17: 4107-9 (1997), and angiogenesis assays such as induction of vascularization of the chick chorioallantoic membrane or induction of vascular endothelial cell migration as described in Ribatta et al., Intl. J. Dev. Biol., 40: 1189-

97 (1999) and Li et al., Clin. Exp. Metastasis, 17:423-9 (1999), respectively. Suitable tumor cells lines are available, e.g. from American Type Tissue Culture Collection catalogs.

4.10.12 RECEPTOR/LIGAND ACTIVITY

A polypeptide of the present invention may also demonstrate activity as receptor, receptor ligand or inhibitor or agonist of receptor/ligand interactions. A polynucleotide of the invention can encode a polypeptide exhibiting such characteristics. Examples of such receptors and ligands include, without limitation, cytokine receptors and their ligands, receptor kinases and their ligands, receptor phosphatases and their ligands, receptors involved in cell-cell interactions and their ligands (including without limitation, cellular adhesion molecules (such as selectins, integrins and their ligands) and receptor/ligand pairs involved in antigen presentation, antigen recognition and development of cellular and humoral immune responses. Receptors and ligands are also useful for screening of potential peptide or small molecule inhibitors of the relevant receptor/ligand interaction. A protein of the present invention (including, without limitation, fragments of receptors and ligands) may themselves be useful as inhibitors of receptor/ligand interactions.

The activity of a polypeptide of the invention may, among other means, be measured by the following methods:

Suitable assays for receptor-ligand activity include without limitation those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A. M. Kruisbeek, D. H. Margulies, E. M. Shevach, W. Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 7.28, Measurement of Cellular Adhesion under static conditions 7.28.1-7.28.22), Takai et al., Proc. Natl. Acad. Sci. USA 84:6864-6868, 1987; Bierer et al., J. Exp. Med. 168:1145-1156, 1988; Rosenstein et al., J. Exp. Med. 169:149-160 1989; Stoltenborg et al., J. Immunol. Methods 175:59-68, 1994; Stitt et al., Cell 80:661-670, 1995.

By way of example, the polypeptides of the invention may be used as a receptor for a ligand(s) thereby transmitting the biological activity of that ligand(s). Ligands may be identified through binding assays, affinity chromatography, dihybrid screening assays, BIAcore assays, gel overlay assays, or other methods known in the art.

Studies characterizing drugs or proteins as agonist or antagonist or partial agonists or a partial antagonist require the use of other proteins as competing ligands. The polypeptides of the present invention or ligand(s) thereof may be labeled by being coupled to radioisotopes, colorimetric molecules or a toxin molecules by conventional methods. ("Guide

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to Protein Purification" Murray P. Deutscher (ed) Methods in Enzymology Vol. 182 (1990) Academic Press, Inc. San Diego). Examples of radioisotopes include, but are not limited to, tritium and carbon-14. Examples of colorimetric molecules include, but are not limited to, fluorescent molecules such as fluorescamine, or rhodamine or other colorimetric molecules. Examples of toxins include, but are not limited, to ricin.

4.10.13 DRUG SCREENING

This invention is particularly useful for screening chemical compounds by using the novel polypeptides or binding fragments thereof in any of a variety of drug screening techniques. The polypeptides or fragments employed in such a test may either be free in solution, affixed to a solid support, borne on a cell surface or located intracellularly. One method of drug screening utilizes eukaryotic or prokaryotic host cells which are stably transformed with recombinant nucleic acids expressing the polypeptide or a fragment thereof. Drugs are screened against such transformed cells in competitive binding assays. Such cells, either in viable or fixed form, can be used for standard binding assays. One may measure, for example, the formation of complexes between polypeptides of the invention or fragments and the agent being tested or examine the diminution in complex formation between the novel polypeptides and an appropriate cell line, which are well known in the art.

Sources for test compounds that may be screened for ability to bind to or modulate (i.e., increase or decrease) the activity of polypeptides of the invention include (1) inorganic and organic chemical libraries, (2) natural product libraries, and (3) combinatorial libraries comprised of either random or mimetic peptides, oligonucleotides or organic molecules.

Chemical libraries may be readily synthesized or purchased from a number of commercial sources, and may include structural analogs of known compounds or compounds that are identified as "hits" or "leads" via natural product screening.

The sources of natural product libraries are microorganisms (including bacteria and fungi), animals, plants or other vegetation, or marine organisms, and libraries of mixtures for screening may be created by: (1) fermentation and extraction of broths from soil, plant or marine microorganisms or (2) extraction of the organisms themselves. Natural product libraries include polyketides, non-ribosomal peptides, and (non-naturally occurring) variants thereof. For a review, see *Science 282*:63-68 (1998).

Combinatorial libraries are composed of large numbers of peptides, oligonucleotides or organic compounds and can be readily prepared by traditional automated synthesis

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methods, PCR, cloning or proprietary synthetic methods. Of particular interest are peptide and oligonucleotide combinatorial libraries. Still other libraries of interest include peptide, protein, peptidomimetic, multiparallel synthetic collection, recombinatorial, and polypeptide libraries. For a review of combinatorial chemistry and libraries created therefrom, see Myers, Curr. Opin. Biotechnol. 8:701-707 (1997). For reviews and examples of peptidomimetic libraries, see Al-Obeidi et al., Mol. Biotechnol, 9(3):205-23 (1998); Hruby et al., Curr Opin Chem Biol, 1(1):114-19 (1997); Dorner et al., Bioorg Med Chem, 4(5):709-15 (1996) (alkylated dipeptides).

Identification of modulators through use of the various libraries described herein permits modification of the candidate "hit" (or "lead") to optimize the capacity of the "hit" to bind a polypeptide of the invention. The molecules identified in the binding assay are then tested for antagonist or agonist activity in *in vivo* tissue culture or animal models that are well known in the art. In brief, the molecules are titrated into a plurality of cell cultures or animals and then tested for either cell/animal death or prolonged survival of the animal/cells.

The binding molecules thus identified may be complexed with toxins, e.g., ricin or cholera, or with other compounds that are toxic to cells such as radioisotopes. The toxin-binding molecule complex is then targeted to a tumor or other cell by the specificity of the binding molecule for a polypeptide of the invention. Alternatively, the binding molecules may be complexed with imaging agents for targeting and imaging purposes.

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4.10.14 ASSAY FOR RECEPTOR ACTIVITY

The invention also provides methods to detect specific binding of a polypeptide e.g. a ligand or a receptor. The art provides numerous assays particularly useful for identifying previously unknown binding partners for receptor polypeptides of the invention. For example, expression cloning using mammalian or bacterial cells, or dihybrid screening assays can be used to identify polynucleotides encoding binding partners. As another example, affinity chromatography with the appropriate immobilized polypeptide of the invention can be used to isolate polypeptides that recognize and bind polypeptides of the invention. There are a number of different libraries used for the identification of compounds, and in particular small molecules, that modulate (i.e., increase or decrease) biological activity of a polypeptide of the invention. Ligands for receptor polypeptides of the invention can also be identified by adding exogenous ligands, or cocktails of ligands to two cells populations that are genetically identical except for the expression of the receptor of the invention: one cell population

expresses the receptor of the invention whereas the other does not. The response of the two cell populations to the addition of ligands(s) are then compared. Alternatively, an expression library can be co-expressed with the polypeptide of the invention in cells and assayed for an autocrine response to identify potential ligand(s). As still another example, BIAcore assays, gel overlay assays, or other methods known in the art can be used to identify binding partner polypeptides, including, (1) organic and inorganic chemical libraries, (2) natural product libraries, and (3) combinatorial libraries comprised of random peptides, oligonucleotides or organic molecules.

The role of downstream intracellular signaling molecules in the signaling cascade of the polypeptide of the invention can be determined. For example, a chimeric protein in which the cytoplasmic domain of the polypeptide of the invention is fused to the extracellular portion of a protein, whose ligand has been identified, is produced in a host cell. The cell is then incubated with the ligand specific for the extracellular portion of the chimeric protein, thereby activating the chimeric receptor. Known downstream proteins involved in intracellular signaling can then be assayed for expected modifications i.e. phosphorylation. Other methods known to those in the art can also be used to identify signaling molecules involved in receptor activity.

4.10.15 ANTI-INFLAMMATORY ACTIVITY

Compositions of the present invention may also exhibit anti-inflammatory activity. The anti-inflammatory activity may be achieved by providing a stimulus to cells involved in the inflammatory response, by inhibiting or promoting cell-cell interactions (such as, for example, cell adhesion), by inhibiting or promoting chemotaxis of cells involved in the inflammatory process, inhibiting or promoting cell extravasation, or by stimulating or suppressing production of other factors which more directly inhibit or promote an inflammatory response. Compositions with such activities can be used to treat inflammatory conditions including chronic or acute conditions), including without limitation intimation associated with infection (such as septic shock, sepsis or systemic inflammatory response syndrome (SIRS)), ischemia-reperfusion injury, endotoxin lethality, arthritis, complement-mediated hyperacute rejection, nephritis, cytokine or chemokine-induced lung injury, inflammatory bowel disease, Crohn's disease or resulting from over production of cytokines such as TNF or IL-1. Compositions of the invention may also be useful to treat anaphylaxis and hypersensitivity to an antigenic substance or material. Compositions of this

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invention may be utilized to prevent or treat conditions such as, but not limited to, sepsis, acute pancreatitis, endotoxin shock, cytokine induced shock, rheumatoid arthritis, chronic inflammatory arthritis, pancreatic cell damage from diabetes mellitus type 1, graft versus host disease, inflammatory bowel disease, inflamation associated with pulmonary disease, other autoimmune disease or inflammatory disease, an antiproliferative agent such as for acute or chronic mylegenous leukemia or in the prevention of premature labor secondary to intrauterine infections.

4.10.16 LEUKEMIAS

Leukemias and related disorders may be treated or prevented by administration of a therapeutic that promotes or inhibits function of the polynucleotides and/or polypeptides of the invention. Such leukemias and related disorders include but are not limited to acute leukemia, acute lymphocytic leukemia, acute myelocytic leukemia, myeloblastic, promyelocytic, myelomonocytic, monocytic, erythroleukemia, chronic leukemia, chronic myelocytic (granulocytic) leukemia and chronic lymphocytic leukemia (for a review of such disorders, see Fishman et al., 1985, Medicine, 2d Ed., J.B. Lippincott Co., Philadelphia).

4.10.17 NERVOUS SYSTEM DISORDERS

Nervous system disorders, involving cell types which can be tested for efficacy of intervention with compounds that modulate the activity of the polynucleotides and/or polypeptides of the invention, and which can be treated upon thus observing an indication of therapeutic utility, include but are not limited to nervous system injuries, and diseases or disorders which result in either a disconnection of axons, a diminution or degeneration of neurons, or demyelination. Nervous system lesions which may be treated in a patient (including human and non-human mammalian patients) according to the invention include but are not limited to the following lesions of either the central (including spinal cord, brain) or peripheral nervous systems:

- (i) traumatic lesions, including lesions caused by physical injury or associated with surgery, for example, lesions which sever a portion of the nervous system, or compression injuries;
- (ii) ischemic lesions, in which a lack of oxygen in a portion of the nervous system results in neuronal injury or death, including cerebral infarction or ischemia, or spinal cord infarction or ischemia;

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(iii) infectious lesions, in which a portion of the nervous system is destroyed or injured as a result of infection, for example, by an abscess or associated with infection by human immunodeficiency virus, herpes zoster, or herpes simplex virus or with Lyme disease, tuberculosis, syphilis;

- (iv) degenerative lesions, in which a portion of the nervous system is destroyed or injured as a result of a degenerative process including but not limited to degeneration associated with Parkinson's disease, Alzheimer's disease, Huntington's chorea, or amyotrophic lateral sclerosis;
- (v) lesions associated with nutritional diseases or disorders, in which a portion of the nervous system is destroyed or injured by a nutritional disorder or disorder of metabolism including but not limited to, vitamin B12 deficiency, folic acid deficiency, Wernicke disease, tobacco-alcohol amblyopia, Marchiafava-Bignami disease (primary degeneration of the corpus callosum), and alcoholic cerebellar degeneration;
- (vi) neurological lesions associated with systemic diseases including but not limited to diabetes (diabetic neuropathy, Bell's palsy), systemic lupus erythematosus, carcinoma, or sarcoidosis;
- (vii) lesions caused by toxic substances including alcohol, lead, or particular neurotoxins; and
- (viii) demyelinated lesions in which a portion of the nervous system is destroyed or injured by a demyelinating disease including but not limited to multiple sclerosis, human immunodeficiency virus-associated myelopathy, transverse myelopathy or various etiologies, progressive multifocal leukoencephalopathy, and central pontine myelinolysis.

Therapeutics which are useful according to the invention for treatment of a nervous system disorder may be selected by testing for biological activity in promoting the survival or differentiation of neurons. For example, and not by way of limitation, therapeutics which elicit any of the following effects may be useful according to the invention:

- (i) increased survival time of neurons in culture;
- (ii) increased sprouting of neurons in culture or in vivo;
- (iii) increased production of a neuron-associated molecule in culture or *in vivo*, e.g., choline acetyltransferase or acetylcholinesterase with respect to motor neurons; or
 - (iv) decreased symptoms of neuron dysfunction in vivo.

Such effects may be measured by any method known in the art. In preferred, non-limiting embodiments, increased survival of neurons may be measured by the method set

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forth in Arakawa et al. (1990, J. Neurosci. 10:3507-3515); increased sprouting of neurons may be detected by methods set forth in Pestronk et al. (1980, Exp. Neurol. 70:65-82) or Brown et al. (1981, Ann. Rev. Neurosci. 4:17-42); increased production of neuron-associated molecules may be measured by bioassay, enzymatic assay, antibody binding, Northern blot assay, etc., depending on the molecule to be measured; and motor neuron dysfunction may be measured by assessing the physical manifestation of motor neuron disorder, e.g., weakness, motor neuron conduction velocity, or functional disability.

In specific embodiments, motor neuron disorders that may be treated according to the invention include but are not limited to disorders such as infarction, infection, exposure to toxin, trauma, surgical damage, degenerative disease or malignancy that may affect motor neurons as well as other components of the nervous system, as well as disorders that selectively affect neurons such as amyotrophic lateral sclerosis, and including but not limited to progressive spinal muscular atrophy, progressive bulbar palsy, primary lateral sclerosis, infantile and juvenile muscular atrophy, progressive bulbar paralysis of childhood (Fazio-Londe syndrome), poliomyelitis and the post polio syndrome, and Hereditary Motorsensory Neuropathy (Charcot-Marie-Tooth Disease).

4.10.18 OTHER ACTIVITIES

A polypeptide of the invention may also exhibit one or more of the following additional activities or effects: inhibiting the growth, infection or function of, or killing, infectious agents, including, without limitation, bacteria, viruses, fungi and other parasites; effecting (suppressing or enhancing) bodily characteristics, including, without limitation, height, weight, hair color, eye color, skin, fat to lean ratio or other tissue pigmentation, or organ or body part size or shape (such as, for example, breast augmentation or diminution, change in bone form or shape); effecting biorhythms or circadian cycles or rhythms; effecting the fertility of male or female subjects; effecting the metabolism, catabolism, anabolism, processing, utilization, storage or elimination of dietary fat, lipid, protein, carbohydrate, vitamins, minerals, co-factors or other nutritional factors or component(s); effecting behavioral characteristics, including, without limitation, appetite, libido, stress, cognition (including cognitive disorders), depression (including depressive disorders) and violent behaviors; providing analgesic effects or other pain reducing effects; promoting differentiation and growth of embryonic stem cells in lineages other than hematopoietic lineages; hormonal or endocrine activity; in the case of enzymes, correcting deficiencies of

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the enzyme and treating deficiency-related diseases; treatment of hyperproliferative disorders (such as, for example, psoriasis); immunoglobulin-like activity (such as, for example, the ability to bind antigens or complement); and the ability to act as an antigen in a vaccine composition to raise an immune response against such protein or another material or entity which is cross-reactive with such protein.

4.10.19 IDENTIFICATION OF POLYMORPHISMS

The demonstration of polymorphisms makes possible the identification of such polymorphisms in human subjects and the pharmacogenetic use of this information for diagnosis and treatment. Such polymorphisms may be associated with, e.g., differential predisposition or susceptibility to various disease states (such as disorders involving inflammation or immune response) or a differential response to drug administration, and this genetic information can be used to tailor preventive or therapeutic treatment appropriately. For example, the existence of a polymorphism associated with a predisposition to inflammation or autoimmune disease makes possible the diagnosis of this condition in humans by identifying the presence of the polymorphism.

Polymorphisms can be identified in a variety of ways known in the art which all generally involve obtaining a sample from a patient, analyzing DNA from the sample, optionally involving isolation or amplification of the DNA, and identifying the presence of the polymorphism in the DNA. For example, PCR may be used to amplify an appropriate fragment of genomic DNA which may then be sequenced. Alternatively, the DNA may be subjected to allele-specific oligonucleotide hybridization (in which appropriate oligonucleotides are hybridized to the DNA under conditions permitting detection of a single base mismatch) or to a single nucleotide extension assay (in which an oligonucleotide that hybridizes immediately adjacent to the position of the polymorphism is extended with one or more labeled nucleotides). In addition, traditional restriction fragment length polymorphism analysis (using restriction enzymes that provide differential digestion of the genomic DNA depending on the presence or absence of the polymorphism) may be performed. Arrays with nucleotide sequences of the present invention can be used to detect polymorphisms. The array can comprise modified nucleotide sequences of the present invention in order to detect the nucleotide sequences of the present invention. In the alternative, any one of the nucleotide sequences of the present invention can be placed on the array to detect changes from those sequences.

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Alternatively a polymorphism resulting in a change in the amino acid sequence could also be detected by detecting a corresponding change in amino acid sequence of the protein, e.g., by an antibody specific to the variant sequence.

4.10.20 ARTHRITIS AND INFLAMMATION

The immunosuppressive effects of the compositions of the invention against rheumatoid arthritis is determined in an experimental animal model system. The experimental model system is adjuvant induced arthritis in rats, and the protocol is described by J. Holoshitz, et at., 1983, Science, 219:56, or by B. Waksman et al., 1963, Int. Arch. Allergy Appl. Immunol., 23:129. Induction of the disease can be caused by a single injection, generally intradermally, of a suspension of killed Mycobacterium tuberculosis in complete Freund's adjuvant (CFA). The route of injection can vary, but rats may be injected at the base of the tail with an adjuvant mixture. The polypeptide is administered in phosphate buffered solution (PBS) at a dose of about 1-5 mg/kg. The control consists of administering PBS only.

The procedure for testing the effects of the test compound would consist of intradermally injecting killed Mycobacterium tuberculosis in CFA followed by immediately administering the test compound and subsequent treatment every other day until day 24. At 14, 15, 18, 20, 22, and 24 days after injection of Mycobacterium CFA, an overall arthritis score may be obtained as described by J. Holoskitz above. An analysis of the data would reveal that the test compound would have a dramatic affect on the swelling of the joints as measured by a decrease of the arthritis score.

4.11 THERAPEUTIC METHODS

The compositions (including polypeptide fragments, analogs, variants and antibodies or other binding partners or modulators including antisense polynucleotides) of the invention have numerous applications in a variety of therapeutic methods. Examples of therapeutic applications include, but are not limited to, those exemplified herein.

4.11.1 EXAMPLE

One embodiment of the invention is the administration of an effective amount of the polypeptides or other composition of the invention to individuals affected by a disease or disorder that can be modulated by regulating the peptides of the invention. While the mode of administration is not particularly important, parenteral administration is preferred. An

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exemplary mode of administration is to deliver an intravenous bolus. The dosage of the polypeptides or other composition of the invention will normally be determined by the prescribing physician. It is to be expected that the dosage will vary according to the age, weight, condition and response of the individual patient. Typically, the amount of polypeptide administered per dose will be in the range of about $0.01\mu g/kg$ to 100 mg/kg of body weight, with the preferred dose being about $0.1\mu g/kg$ to 10 mg/kg of patient body weight. For parenteral administration, polypeptides of the invention will be formulated in an injectable form combined with a pharmaceutically acceptable parenteral vehicle. Such vehicles are well known in the art and examples include water, saline, Ringer's solution, dextrose solution, and solutions consisting of small amounts of the human serum albumin. The vehicle may contain minor amounts of additives that maintain the isotonicity and stability of the polypeptide or other active ingredient. The preparation of such solutions is within the skill of the art.

4.12 PHARMACEUTICAL FORMULATIONS AND ROUTES OF ADMINISTRATION

A protein or other composition of the present invention (from whatever source derived, including without limitation from recombinant and non-recombinant sources and including antibodies and other binding partners of the polypeptides of the invention) may be administered to a patient in need, by itself, or in pharmaceutical compositions where it is mixed with suitable carriers or excipient(s) at doses to treat or ameliorate a variety of disorders. Such a composition may optionally contain (in addition to protein or other active ingredient and a carrier) diluents, fillers, salts, buffers, stabilizers, solubilizers, and other materials well known in the art. The term "pharmaceutically acceptable" means a non-toxic material that does not interfere with the effectiveness of the biological activity of the active ingredient(s). The characteristics of the carrier will depend on the route of administration. The pharmaceutical composition of the invention may also contain cytokines, lymphokines, or other hematopoietic factors such as M-CSF, GM-CSF, TNF, IL-1, IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-11, IL-12, IL-13, IL-14, IL-15, IFN, TNF0, TNF1, TNF2, G-CSF, Meg-CSF, thrombopoietin, stem cell factor, and erythropoietin. In further compositions, proteins of the invention may be combined with other agents beneficial to the treatment of the disease or disorder in question. These agents include various growth factors such as epidermal growth factor (EGF), platelet-derived growth factor (PDGF), transforming

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growth factors (TGF- α and TGF- β), insulin-like growth factor (IGF), as well as cytokines described herein.

The pharmaceutical composition may further contain other agents which either enhance the activity of the protein or other active ingredient or complement its activity or use in treatment. Such additional factors and/or agents may be included in the pharmaceutical composition to produce a synergistic effect with protein or other active ingredient of the invention, or to minimize side effects. Conversely, protein or other active ingredient of the present invention may be included in formulations of the particular clotting factor, cytokine, lymphokine, other hematopoietic factor, thrombolytic or anti-thrombotic factor, or anti-inflammatory agent to minimize side effects of the clotting factor, cytokine, lymphokine, other hematopoietic factor, thrombolytic or anti-thrombotic factor, or anti-inflammatory agent (such as IL-1Ra, IL-1 Hy1, IL-1 Hy2, anti-TNF, corticosteroids, immunosuppressive agents). A protein of the present invention may be active in multimers (e.g., heterodimers or homodimers) or complexes with itself or other proteins. As a result, pharmaceutical compositions of the invention may comprise a protein of the invention in such multimeric or complexed form.

As an alternative to being included in a pharmaceutical composition of the invention including a first protein, a second protein or a therapeutic agent may be concurrently administered with the first protein (e.g., at the same time, or at differing times provided that therapeutic concentrations of the combination of agents is achieved at the treatment site). Techniques for formulation and administration of the compounds of the instant application may be found in "Remington's Pharmaceutical Sciences," Mack Publishing Co., Easton, PA, latest edition. A therapeutically effective dose further refers to that amount of the compound sufficient to result in amelioration of symptoms, e.g., treatment, healing, prevention or amelioration of the relevant medical condition, or an increase in rate of treatment, healing, prevention or amelioration of such conditions. When applied to an individual active ingredient, administered alone, a therapeutically effective dose refers to that ingredient alone. When applied to a combination, a therapeutically effective dose refers to combined amounts of the active ingredients that result in the therapeutic effect, whether administered in combination, serially or simultaneously.

In practicing the method of treatment or use of the present invention, a therapeutically effective amount of protein or other active ingredient of the present invention is administered to a mammal having a condition to be treated. Protein or other active ingredient of the

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present invention may be administered in accordance with the method of the invention either alone or in combination with other therapies such as treatments employing cytokines, lymphokines or other hematopoietic factors. When co- administered with one or more cytokines, lymphokines or other hematopoietic factors, protein or other active ingredient of the present invention may be administered either simultaneously with the cytokine(s), lymphokine(s), other hematopoietic factor(s), thrombolytic or anti-thrombotic factors, or sequentially. If administered sequentially, the attending physician will decide on the appropriate sequence of administering protein or other active ingredient of the present invention in combination with cytokine(s), lymphokine(s), other hematopoietic factor(s), thrombolytic or anti-thrombotic factors.

4.12.1 ROUTES OF ADMINISTRATION

Suitable routes of administration may, for example, include oral, rectal, transmucosal, or intestinal administration; parenteral delivery, including intramuscular, subcutaneous, intramedullary injections, as well as intrathecal, direct intraventricular, intravenous, intraperitoneal, intranasal, or intraocular injections. Administration of protein or other active ingredient of the present invention used in the pharmaceutical composition or to practice the method of the present invention can be carried out in a variety of conventional ways, such as oral ingestion, inhalation, topical application or cutaneous, subcutaneous, intraperitoneal, parenteral or intravenous injection. Intravenous administration to the patient is preferred.

Alternately, one may administer the compound in a local rather than systemic manner, for example, via injection of the compound directly into a arthritic joints or in fibrotic tissue, often in a depot or sustained release formulation. In order to prevent the scarring process frequently occurring as complication of glaucoma surgery, the compounds may be administered topically, for example, as eye drops. Furthermore, one may administer the drug in a targeted drug delivery system, for example, in a liposome coated with a specific antibody, targeting, for example, arthritic or fibrotic tissue. The liposomes will be targeted to and taken up selectively by the afflicted tissue.

The polypeptides of the invention are administered by any route that delivers an effective dosage to the desired site of action. The determination of a suitable route of administration and an effective dosage for a particular indication is within the level of skill in the art. Preferably for wound treatment, one administers the therapeutic compound directly to the site. Suitable dosage ranges for the polypeptides of the invention can be extrapolated

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from these dosages or from similar studies in appropriate animal models. Dosages can then be adjusted as necessary by the clinician to provide maximal therapeutic benefit.

4.12.2 COMPOSITIONS/FORMULATIONS

Pharmaceutical compositions for use in accordance with the present invention thus may be formulated in a conventional manner using one or more physiologically acceptable carriers comprising excipients and auxiliaries which facilitate processing of the active compounds into preparations which can be used pharmaceutically. These pharmaceutical compositions may be manufactured in a manner that is itself known, e.g., by means of conventional mixing, dissolving, granulating, dragee-making, levigating, emulsifying, encapsulating, entrapping or lyophilizing processes. Proper formulation is dependent upon the route of administration chosen. When a therapeutically effective amount of protein or other active ingredient of the present invention is administered orally, protein or other active ingredient of the present invention will be in the form of a tablet, capsule, powder, solution or elixir. When administered in tablet form, the pharmaceutical composition of the invention may additionally contain a solid carrier such as a gelatin or an adjuvant. The tablet, capsule, and powder contain from about 5 to 95% protein or other active ingredient of the present invention, and preferably from about 25 to 90% protein or other active ingredient of the present invention. When administered in liquid form, a liquid carrier such as water, petroleum, oils of animal or plant origin such as peanut oil, mineral oil, soybean oil, or sesame oil, or synthetic oils may be added. The liquid form of the pharmaceutical composition may further contain physiological saline solution, dextrose or other saccharide solution, or glycols such as ethylene glycol, propylene glycol or polyethylene glycol. When administered in liquid form, the pharmaceutical composition contains from about 0.5 to 90% by weight of protein or other active ingredient of the present invention, and preferably from about 1 to 50% protein or other active ingredient of the present invention.

When a therapeutically effective amount of protein or other active ingredient of the present invention is administered by intravenous, cutaneous or subcutaneous injection, protein or other active ingredient of the present invention will be in the form of a pyrogen-free, parenterally acceptable aqueous solution. The preparation of such parenterally acceptable protein or other active ingredient solutions, having due regard to pH, isotonicity, stability, and the like, is within the skill in the art. A preferred pharmaceutical composition for intravenous, cutaneous, or subcutaneous injection should contain, in addition to protein or

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other active ingredient of the present invention, an isotonic vehicle such as Sodium Chloride Injection, Ringer's Injection, Dextrose Injection, Dextrose and Sodium Chloride Injection, Lactated Ringer's Injection, or other vehicle as known in the art. The pharmaceutical composition of the present invention may also contain stabilizers, preservatives, buffers, antioxidants, or other additives known to those of skill in the art. For injection, the agents of the invention may be formulated in aqueous solutions, preferably in physiologically compatible buffers such as Hanks's solution, Ringer's solution, or physiological saline buffer. For transmucosal administration, penetrants appropriate to the barrier to be permeated are used in the formulation. Such penetrants are generally known in the art.

For oral administration, the compounds can be formulated readily by combining the active compounds with pharmaceutically acceptable carriers well known in the art. Such carriers enable the compounds of the invention to be formulated as tablets, pills, dragees, capsules, liquids, gels, syrups, slurries, suspensions and the like, for oral ingestion by a patient to be treated. Pharmaceutical preparations for oral use can be obtained from a solid excipient, optionally grinding a resulting mixture, and processing the mixture of granules, after adding suitable auxiliaries, if desired, to obtain tablets or dragee cores. Suitable excipients are, in particular, fillers such as sugars, including lactose, sucrose, mannitol, or sorbitol; cellulose preparations such as, for example, maize starch, wheat starch, rice starch, potato starch, gelatin, gum tragacanth, methyl cellulose, hydroxypropylmethyl-cellulose, sodium carboxymethylcellulose, and/or polyvinylpyrrolidone (PVP). If desired, disintegrating agents may be added, such as the cross-linked polyvinyl pyrrolidone, agar, or alginic acid or a salt thereof such as sodium alginate. Dragee cores are provided with suitable coatings. For this purpose, concentrated sugar solutions may be used, which may optionally contain gum arabic, talc, polyvinyl pyrrolidone, carbopol gel, polyethylene glycol, and/or titanium dioxide, lacquer solutions, and suitable organic solvents or solvent mixtures. Dyestuffs or pigments may be added to the tablets or dragee coatings for identification or to characterize different combinations of active compound doses.

Pharmaceutical preparations which can be used orally include push-fit capsules made of gelatin, as well as soft, sealed capsules made of gelatin and a plasticizer, such as glycerol or sorbitol. The push-fit capsules can contain the active ingredients in admixture with filler such as lactose, binders such as starches, and/or lubricants such as talc or magnesium stearate and, optionally, stabilizers. In soft capsules, the active compounds may be dissolved or suspended in suitable liquids, such as fatty oils, liquid paraffin, or liquid polyethylene

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glycols. In addition, stabilizers may be added. All formulations for oral administration should be in dosages suitable for such administration. For buccal administration, the compositions may take the form of tablets or lozenges formulated in conventional manner.

For administration by inhalation, the compounds for use according to the present invention are conveniently delivered in the form of an aerosol spray presentation from pressurized packs or a nebuliser, with the use of a suitable propellant, e.g., dichlorodifluoromethane, trichlorofluoromethane, dichlorotetrafluoroethane, carbon dioxide or other suitable gas. In the case of a pressurized aerosol the dosage unit may be determined by providing a valve to deliver a metered amount. Capsules and cartridges of, e.g., gelatin for use in an inhaler or insufflator may be formulated containing a powder mix of the compound and a suitable powder base such as lactose or starch. The compounds may be formulated for parenteral administration by injection, e.g., by bolus injection or continuous infusion. Formulations for injection may be presented in unit dosage form, e.g., in ampules or in multi-dose containers, with an added preservative. The compositions may take such forms as suspensions, solutions or emulsions in oily or aqueous vehicles, and may contain formulatory agents such as suspending, stabilizing and/or dispersing agents.

Pharmaceutical formulations for parenteral administration include aqueous solutions of the active compounds in water-soluble form. Additionally, suspensions of the active compounds may be prepared as appropriate oily injection suspensions. Suitable lipophilic solvents or vehicles include fatty oils such as sesame oil, or synthetic fatty acid esters, such as ethyl oleate or triglycerides, or liposomes. Aqueous injection suspensions may contain substances which increase the viscosity of the suspension, such as sodium carboxymethyl cellulose, sorbitol, or dextran. Optionally, the suspension may also contain suitable stabilizers or agents which increase the solubility of the compounds to allow for the preparation of highly concentrated solutions. Alternatively, the active ingredient may be in powder form for constitution with a suitable vehicle, e.g., sterile pyrogen-free water, before use.

The compounds may also be formulated in rectal compositions such as suppositories or retention enemas, e.g., containing conventional suppository bases such as cocoa butter or other glycerides. In addition to the formulations described previously, the compounds may also be formulated as a depot preparation. Such long acting formulations may be administered by implantation (for example subcutaneously or intramuscularly) or by intramuscular injection. Thus, for example, the compounds may be formulated with suitable

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polymeric or hydrophobic materials (for example as an emulsion in an acceptable oil) or ion exchange resins, or as sparingly soluble derivatives, for example, as a sparingly soluble salt.

A pharmaceutical carrier for the hydrophobic compounds of the invention is a cosolvent system comprising benzyl alcohol, a nonpolar surfactant, a water-miscible organic polymer, and an aqueous phase. The co-solvent system may be the VPD co-solvent system. VPD is a solution of 3% w/v benzyl alcohol, 8% w/v of the nonpolar surfactant polysorbate 80, and 65% w/v polyethylene glycol 300, made up to volume in absolute ethanol. The VPD co-solvent system (VPD:5W) consists of VPD diluted 1:1 with a 5% dextrose in water solution. This co-solvent system dissolves hydrophobic compounds well, and itself produces low toxicity upon systemic administration. Naturally, the proportions of a co-solvent system may be varied considerably without destroying its solubility and toxicity characteristics. Furthermore, the identity of the co-solvent components may be varied: for example, other low-toxicity nonpolar surfactants may be used instead of polysorbate 80; the fraction size of polyethylene glycol may be varied; other biocompatible polymers may replace polyethylene glycol, e.g. polyvinyl pyrrolidone; and other sugars or polysaccharides may substitute for dextrose. Alternatively, other delivery systems for hydrophobic pharmaceutical compounds may be employed. Liposomes and emulsions are well known examples of delivery vehicles or carriers for hydrophobic drugs. Certain organic solvents such as dimethylsulfoxide also may be employed, although usually at the cost of greater toxicity. Additionally, the compounds may be delivered using a sustained-release system, such as semipermeable matrices of solid hydrophobic polymers containing the therapeutic agent. Various types of sustained-release materials have been established and are well known by those skilled in the art. Sustained-release capsules may, depending on their chemical nature, release the compounds for a few weeks up to over 100 days. Depending on the chemical nature and the biological stability of the therapeutic reagent, additional strategies for protein or other active ingredient stabilization may be employed.

The pharmaceutical compositions also may comprise suitable solid or gel phase carriers or excipients. Examples of such carriers or excipients include but are not limited to calcium carbonate, calcium phosphate, various sugars, starches, cellulose derivatives, gelatin, and polymers such as polyethylene glycols. Many of the active ingredients of the invention may be provided as salts with pharmaceutically compatible counter ions. Such pharmaceutically acceptable base addition salts are those salts which retain the biological effectiveness and properties of the free acids and which are obtained by reaction with

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inorganic or organic bases such as sodium hydroxide, magnesium hydroxide, ammonia, trialkylamine, dialkylamine, monoalkylamine, dibasic amino acids, sodium acetate, potassium benzoate, triethanol amine and the like.

The pharmaceutical composition of the invention may be in the form of a complex of the protein(s) or other active ingredient(s) of present invention along with protein or peptide antigens. The protein and/or peptide antigen will deliver a stimulatory signal to both B and T lymphocytes. B lymphocytes will respond to antigen through their surface immunoglobulin receptor. T lymphocytes will respond to antigen through the T cell receptor (TCR) following presentation of the antigen by MHC proteins. MHC and structurally related proteins including those encoded by class I and class II MHC genes on host cells will serve to present the peptide antigen(s) to T lymphocytes. The antigen components could also be supplied as purified MHC-peptide complexes alone or with co-stimulatory molecules that can directly signal T cells. Alternatively antibodies able to bind surface immunoglobulin and other molecules on B cells as well as antibodies able to bind the TCR and other molecules on T cells can be combined with the pharmaceutical composition of the invention.

The pharmaceutical composition of the invention may be in the form of a liposome in which protein of the present invention is combined, in addition to other pharmaceutically acceptable carriers, with amphipathic agents such as lipids which exist in aggregated form as micelles, insoluble monolayers, liquid crystals, or lamellar layers in aqueous solution. Suitable lipids for liposomal formulation include, without limitation, monoglycerides, diglycerides, sulfatides, lysolecithins, phospholipids, saponin, bile acids, and the like. Preparation of such liposomal formulations is within the level of skill in the art, as disclosed, for example, in U.S. Patent Nos. 4,235,871; 4,501,728; 4,837,028; and 4,737,323, all of which are incorporated herein by reference.

The amount of protein or other active ingredient of the present invention in the pharmaceutical composition of the present invention will depend upon the nature and severity of the condition being treated, and on the nature of prior treatments which the patient has undergone. Ultimately, the attending physician will decide the amount of protein or other active ingredient of the present invention with which to treat each individual patient. Initially, the attending physician will administer low doses of protein or other active ingredient of the present invention and observe the patient's response. Larger doses of protein or other active ingredient of the present invention may be administered until the optimal therapeutic effect is obtained for the patient, and at that point the dosage is not

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increased further. It is contemplated that the various pharmaceutical compositions used to practice the method of the present invention should contain about 0.01 µg to about 100 mg (preferably about 0.1 µg to about 10 mg, more preferably about 0.1 µg to about 1 mg) of protein or other active ingredient of the present invention per kg body weight. For compositions of the present invention which are useful for bone, cartilage, tendon or ligament regeneration, the therapeutic method includes administering the composition topically, systematically, or locally as an implant or device. When administered, the therapeutic composition for use in this invention is, of course, in a pyrogen-free, physiologically acceptable form. Further, the composition may desirably be encapsulated or injected in a viscous form for delivery to the site of bone, cartilage or tissue damage. Topical administration may be suitable for wound healing and tissue repair. Therapeutically useful agents other than a protein or other active ingredient of the invention which may also optionally be included in the composition as described above, may alternatively or additionally, be administered simultaneously or sequentially with the composition in the methods of the invention. Preferably for bone and/or cartilage formation, the composition would include a matrix capable of delivering the protein-containing or other active ingredient-containing composition to the site of bone and/or cartilage damage, providing a structure for the developing bone and cartilage and optimally capable of being resorbed into the body. Such matrices may be formed of materials presently in use for other implanted medical applications.

The choice of matrix material is based on biocompatibility, biodegradability, mechanical properties, cosmetic appearance and interface properties. The particular application of the compositions will define the appropriate formulation. Potential matrices for the compositions may be biodegradable and chemically defined calcium sulfate, tricalcium phosphate, hydroxyapatite, polylactic acid, polyglycolic acid and polyanhydrides. Other potential materials are biodegradable and biologically well-defined, such as bone or dermal collagen. Further matrices are comprised of pure proteins or extracellular matrix components. Other potential matrices are nonbiodegradable and chemically defined, such as sintered hydroxyapatite, bioglass, aluminates, or other ceramics. Matrices may be comprised of combinations of any of the above mentioned types of material, such as polylactic acid and hydroxyapatite or collagen and tricalcium phosphate. The bioceramics may be altered in composition, such as in calcium-aluminate-phosphate and processing to alter pore size, particle size, particle shape, and biodegradability. Presently preferred is a 50:50 (mole

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weight) copolymer of lactic acid and glycolic acid in the form of porous particles having diameters ranging from 150 to 800 microns. In some applications, it will be useful to utilize a sequestering agent, such as carboxymethyl cellulose or autologous blood clot, to prevent the protein compositions from disassociating from the matrix.

A preferred family of sequestering agents is cellulosic materials such as alkylcelluloses (including hydroxyalkylcelluloses), including methylcellulose, ethylcellulose, hydroxyethylcellulose, hydroxypropylcellulose, hydroxypropyl-methylcellulose, and carboxymethylcellulose, the most preferred being cationic salts of carboxymethylcellulose (CMC). Other preferred sequestering agents include hyaluronic acid, sodium alginate, poly(ethylene glycol), polyoxyethylene oxide, carboxyvinyl polymer and poly(vinyl alcohol). The amount of sequestering agent useful herein is 0.5-20 wt %, preferably 1-10 wt % based on total formulation weight, which represents the amount necessary to prevent desorption of the protein from the polymer matrix and to provide appropriate handling of the composition, yet not so much that the progenitor cells are prevented from infiltrating the matrix, thereby providing the protein the opportunity to assist the osteogenic activity of the progenitor cells. In further compositions, proteins or other active ingredients of the invention may be combined with other agents beneficial to the treatment of the bone and/or cartilage defect, wound, or tissue in question. These agents include various growth factors such as epidermal growth factor (EGF), platelet derived growth factor (PDGF), transforming growth factors (TGF-α and TGF-β), and insulin-like growth factor (IGF).

The therapeutic compositions are also presently valuable for veterinary applications. Particularly domestic animals and thoroughbred horses, in addition to humans, are desired patients for such treatment with proteins or other active ingredients of the present invention. The dosage regimen of a protein-containing pharmaceutical composition to be used in tissue regeneration will be determined by the attending physician considering various factors which modify the action of the proteins, e.g., amount of tissue weight desired to be formed, the site of damage, the condition of the damaged tissue, the size of a wound, type of damaged tissue (e.g., bone), the patient's age, sex, and diet, the severity of any infection, time of administration and other clinical factors. The dosage may vary with the type of matrix used in the reconstitution and with inclusion of other proteins in the pharmaceutical composition. For example, the addition of other known growth factors, such as IGF I (insulin like growth factor I), to the final composition, may also effect the dosage. Progress can be monitored by

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periodic assessment of tissue/bone growth and/or repair, for example, X-rays, histomorphometric determinations and tetracycline labeling.

Polynucleotides of the present invention can also be used for gene therapy. Such polynucleotides can be introduced either in vivo or ex vivo into cells for expression in a mammalian subject. Polynucleotides of the invention may also be administered by other known methods for introduction of nucleic acid into a cell or organism (including, without limitation, in the form of viral vectors or naked DNA). Cells may also be cultured ex vivo in the presence of proteins of the present invention in order to proliferate or to produce a desired effect on or activity in such cells. Treated cells can then be introduced in vivo for therapeutic purposes.

4.12.3 EFFECTIVE DOSAGE

Pharmaceutical compositions suitable for use in the present invention include compositions wherein the active ingredients are contained in an effective amount to achieve its intended purpose. More specifically, a therapeutically effective amount means an amount effective to prevent development of or to alleviate the existing symptoms of the subject being treated. Determination of the effective amount is well within the capability of those skilled in the art, especially in light of the detailed disclosure provided herein. For any compound used in the method of the invention, the therapeutically effective dose can be estimated initially from appropriate in vitro assays. For example, a dose can be formulated in animal models to achieve a circulating concentration range that can be used to more accurately determine useful doses in humans. For example, a dose can be formulated in animal models to achieve a circulating concentration range that includes the IC₅₀ as determined in cell culture (*i.e.*, the concentration of the test compound which achieves a half-maximal inhibition of the protein's biological activity). Such information can be used to more accurately determine useful doses in humans.

A therapeutically effective dose refers to that amount of the compound that results in amelioration of symptoms or a prolongation of survival in a patient. Toxicity and therapeutic efficacy of such compounds can be determined by standard pharmaceutical procedures in cell cultures or experimental animals, e.g., for determining the LD₅₀ (the dose lethal to 50% of the population) and the ED₅₀ (the dose therapeutically effective in 50% of the population). The dose ratio between toxic and therapeutic effects is the therapeutic index and it can be expressed as the ratio between LD₅₀ and ED₅₀. Compounds which exhibit high therapeutic

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indices are preferred. The data obtained from these cell culture assays and animal studies can be used in formulating a range of dosage for use in human. The dosage of such compounds lies preferably within a range of circulating concentrations that include the ED₅₀ with little or no toxicity. The dosage may vary within this range depending upon the dosage form employed and the route of administration utilized. The exact formulation, route of administration and dosage can be chosen by the individual physician in view of the patient's condition. See, e.g., Fingl et al., 1975, in "The Pharmacological Basis of Therapeutics", Ch. 1 p.1. Dosage amount and interval may be adjusted individually to provide plasma levels of the active moiety which are sufficient to maintain the desired effects, or minimal effective concentration (MEC). The MEC will vary for each compound but can be estimated from in vitro data. Dosages necessary to achieve the MEC will depend on individual characteristics and route of administration. However, HPLC assays or bioassays can be used to determine plasma concentrations.

Dosage intervals can also be determined using MEC value. Compounds should be administered using a regimen which maintains plasma levels above the MEC for 10-90% of the time, preferably between 30-90% and most preferably between 50-90%. In cases of local administration or selective uptake, the effective local concentration of the drug may not be related to plasma concentration.

An exemplary dosage regimen for polypeptides or other compositions of the invention will be in the range of about 0.01 μ g/kg to 100 mg/kg of body weight daily, with the preferred dose being about 0.1 μ g/kg to 25 mg/kg of patient body weight daily, varying in adults and children. Dosing may be once daily, or equivalent doses may be delivered at longer or shorter intervals.

The amount of composition administered will, of course, be dependent on the subject being treated, on the subject's age and weight, the severity of the affliction, the manner of administration and the judgment of the prescribing physician.

4.12.4 PACKAGING

The compositions may, if desired, be presented in a pack or dispenser device which may contain one or more unit dosage forms containing the active ingredient. The pack may, for example, comprise metal or plastic foil, such as a blister pack. The pack or dispenser device may be accompanied by instructions for administration. Compositions comprising a compound of the invention formulated in a compatible pharmaceutical carrier may also be

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prepared, placed in an appropriate container, and labeled for treatment of an indicated condition.

4.13 ANTIBODIES

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Also included in the invention are antibodies to proteins, or fragments of proteins of the invention. The term "antibody" as used herein refers to immunoglobulin molecules and immunologically active portions of immunoglobulin (Ig) molecules, i.e., molecules that contain an antigen binding site that specifically binds (immunoreacts with) an antigen. Such antibodies include, but are not limited to, polyclonal, monoclonal, chimeric, single chain, F_{ab} , F_{ab} , and $F_{(ab)2}$ fragments, and an F_{ab} expression library. In general, an antibody molecule obtained from humans relates to any of the classes IgG, IgM, IgA, IgE and IgD, which differ from one another by the nature of the heavy chain present in the molecule. Certain classes have subclasses as well, such as IgG_1 , IgG_2 , and others. Furthermore, in humans, the light chain may be a kappa chain or a lambda chain. Reference herein to antibodies includes a reference to all such classes, subclasses and types of human antibody species.

An isolated related protein of the invention may be intended to serve as an antigen, or a portion or fragment thereof, and additionally can be used as an immunogen to generate antibodies that immunospecifically bind the antigen, using standard techniques for polyclonal and monoclonal antibody preparation. The full-length protein can be used or, alternatively, the invention provides antigenic peptide fragments of the antigen for use as immunogens. An antigenic peptide fragment comprises at least 6 amino acid residues of the amino acid sequence of the full length protein, such as the amino acid sequences shown in SEQ ID NO: 94-186, and encompasses an epitope thereof such that an antibody raised against the peptide forms a specific immune complex with the full length protein or with any fragment that contains the epitope. Preferably, the antigenic peptide comprises at least 10 amino acid residues, or at least 15 amino acid residues, or at least 20 amino acid residues, or at least 30 amino acid residues. Preferred epitopes encompassed by the antigenic peptide are regions of the protein that are located on its surface; commonly these are hydrophilic regions.

In certain embodiments of the invention, at least one epitope encompassed by the antigenic peptide is a region of -related protein that is located on the surface of the protein, e.g., a hydrophilic region. A hydrophobicity analysis of the human related protein sequence will indicate which regions of a related protein are particularly hydrophilic and, therefore, are likely to encode surface residues useful for targeting antibody production. As a means for

targeting antibody production, hydropathy plots showing regions of hydrophilicity and hydrophobicity may be generated by any method well known in the art, including, for example, the Kyte Doolittle or the Hopp Woods methods, either with or without Fourier transformation. See, e.g., Hopp and Woods, 1981, Proc. Nat. Acad. Sci. USA 78: 3824-3828; Kyte and Doolittle 1982, J. Mol. Biol. 157: 105-142, each of which is incorporated herein by reference in its entirety. Antibodies that are specific for one or more domains within an antigenic protein, or derivatives, fragments, analogs or homologs thereof, are also provided herein.

A protein of the invention, or a derivative, fragment, analog, homolog or ortholog thereof, may be utilized as an immunogen in the generation of antibodies that immunospecifically bind these protein components.

Various procedures known within the art may be used for the production of polyclonal or monoclonal antibodies directed against a protein of the invention, or against derivatives, fragments, analogs homologs or orthologs thereof (see, for example, Antibodies: A Laboratory Manual, Harlow E, and Lane D, 1988, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, incorporated herein by reference). Some of these antibodies are discussed below.

4.13.1 POLYCLONAL ANTIBODIES

For the production of polyclonal antibodies, various suitable host animals (e.g., rabbit, goat, mouse or other mammal) may be immunized by one or more injections with the native protein, a synthetic variant thereof, or a derivative of the foregoing. An appropriate immunogenic preparation can contain, for example, the naturally occurring immunogenic protein, a chemically synthesized polypeptide representing the immunogenic protein, or a recombinantly expressed immunogenic protein. Furthermore, the protein may be conjugated to a second protein known to be immunogenic in the mammal being immunized. Examples of such immunogenic proteins include but are not limited to keyhole limpet hemocyanin, serum albumin, bovine thyroglobulin, and soybean trypsin inhibitor. The preparation can further include an adjuvant. Various adjuvants used to increase the immunological response include, but are not limited to, Freund's (complete and incomplete), mineral gels (e.g., aluminum hydroxide), surface active substances (e.g., lysolecithin, pluronic polyols, polyanions, peptides, oil emulsions, dinitrophenol, etc.), adjuvants usable in humans such as Bacille Calmette-Guerin and Corynebacterium parvum, or similar immunostimulatory agents.

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Additional examples of adjuvants which can be employed include MPL-TDM adjuvant (monophosphoryl Lipid A, synthetic trehalose dicorynomycolate).

The polyclonal antibody molecules directed against the immunogenic protein can be isolated from the mammal (e.g., from the blood) and further purified by well known techniques, such as affinity chromatography using protein A or protein G, which provide primarily the IgG fraction of immune serum. Subsequently, or alternatively, the specific antigen which is the target of the immunoglobulin sought, or an epitope thereof, may be immobilized on a column to purify the immune specific antibody by immunoaffinity chromatography. Purification of immunoglobulins is discussed, for example, by D. Wilkinson (The Scientist, published by The Scientist, Inc., Philadelphia PA, Vol. 14, No. 8 (April 17, 2000), pp. 25-28).

4.13.2 MONOCLONAL ANTIBODIES

The term "monoclonal antibody" (MAb) or "monoclonal antibody composition", as used herein, refers to a population of antibody molecules that contain only one molecular species of antibody molecule consisting of a unique light chain gene product and a unique heavy chain gene product. In particular, the complementarity determining regions (CDRs) of the monoclonal antibody are identical in all the molecules of the population. MAbs thus contain an antigen binding site capable of immunoreacting with a particular epitope of the antigen characterized by a unique binding affinity for it.

Monoclonal antibodies can be prepared using hybridoma methods, such as those described by Kohler and Milstein, Nature, 256:495 (1975). In a hybridoma method, a mouse, hamster, or other appropriate host animal, is typically immunized with an immunizing agent to elicit lymphocytes that produce or are capable of producing antibodies that will specifically bind to the immunizing agent. Alternatively, the lymphocytes can be immunized in vitro.

The immunizing agent will typically include the protein antigen, a fragment thereof or a fusion protein thereof. Generally, either peripheral blood lymphocytes are used if cells of human origin are desired, or spleen cells or lymph node cells are used if non-human mammalian sources are desired. The lymphocytes are then fused with an immortalized cell line using a suitable fusing agent, such as polyethylene glycol, to form a hybridoma cell (Goding, Monoclonal Antibodies: Principles and Practice, Academic Press, (1986) pp. 59-103). Immortalized cell lines are usually transformed mammalian cells, particularly

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myeloma cells of rodent, bovine and human origin. Usually, rat or mouse myeloma cell lines are employed. The hybridoma cells can be cultured in a suitable culture medium that preferably contains one or more substances that inhibit the growth or survival of the unfused, immortalized cells. For example, if the parental cells lack the enzyme hypoxanthine guanine phosphoribosyl transferase (HGPRT or HPRT), the culture medium for the hybridomas typically will include hypoxanthine, aminopterin, and thymidine ("HAT medium"), which substances prevent the growth of HGPRT-deficient cells.

Preferred immortalized cell lines are those that fuse efficiently, support stable high level expression of antibody by the selected antibody-producing cells, and are sensitive to a medium such as HAT medium. More preferred immortalized cell lines are murine myeloma lines, which can be obtained, for instance, from the Salk Institute Cell Distribution Center, San Diego, California and the American Type Culture Collection, Manassas, Virginia. Human myeloma and mouse-human heteromyeloma cell lines also have been described for the production of human monoclonal antibodies (Kozbor, <u>J. Immunol.</u>, <u>133</u>:3001 (1984); Brodeur et al., <u>Monoclonal Antibody Production Techniques and Applications</u>, Marcel Dekker, Inc., New York, (1987) pp. 51-63).

The culture medium in which the hybridoma cells are cultured can then be assayed for the presence of monoclonal antibodies directed against the antigen. Preferably, the binding specificity of monoclonal antibodies produced by the hybridoma cells is determined by immunoprecipitation or by an in vitro binding assay, such as radioimmunoassay (RIA) or enzyme-linked immunoabsorbent assay (ELISA). Such techniques and assays are known in the art. The binding affinity of the monoclonal antibody can, for example, be determined by the Scatchard analysis of Munson and Pollard, Anal. Biochem., 107:220 (1980). Preferably, antibodies having a high degree of specificity and a high binding affinity for the target antigen are isolated.

After the desired hybridoma cells are identified, the clones can be subcloned by limiting dilution procedures and grown by standard methods. Suitable culture media for this purpose include, for example, Dulbecco's Modified Eagle's Medium and RPMI-1640 medium. Alternatively, the hybridoma cells can be grown in vivo as ascites in a mammal. The monoclonal antibodies secreted by the subclones can be isolated or purified from the culture medium or ascites fluid by conventional immunoglobulin purification procedures such as, for example, protein A-Sepharose, hydroxylapatite chromatography, gel electrophoresis, dialysis, or affinity chromatography.

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The monoclonal antibodies can also be made by recombinant DNA methods, such as those described in U.S. Patent No. 4,816,567. DNA encoding the monoclonal antibodies of the invention can be readily isolated and sequenced using conventional procedures (e.g., by using oligonucleotide probes that are capable of binding specifically to genes encoding the heavy and light chains of murine antibodies). The hybridoma cells of the invention serve as a preferred source of such DNA. Once isolated, the DNA can be placed into expression vectors, which are then transfected into host cells such as simian COS cells, Chinese hamster ovary (CHO) cells, or myeloma cells that do not otherwise produce immunoglobulin protein, to obtain the synthesis of monoclonal antibodies in the recombinant host cells. The DNA also can be modified, for example, by substituting the coding sequence for human heavy and light chain constant domains in place of the homologous murine sequences (U.S. Patent No. 4,816,567; Morrison, Nature 368, 812-13 (1994)) or by covalently joining to the immunoglobulin coding sequence all or part of the coding sequence for a nonimmunoglobulin polypeptide. Such a non-immunoglobulin polypeptide can be substituted for the constant domains of an antibody of the invention, or can be substituted for the variable domains of one antigen-combining site of an antibody of the invention to create a chimeric bivalent antibody.

4.13.3 HUMANIZED ANTIBODIES

The antibodies directed against the protein antigens of the invention can further comprise humanized antibodies or human antibodies. These antibodies are suitable for administration to humans without engendering an immune response by the human against the administered immunoglobulin. Humanized forms of antibodies are chimeric immunoglobulins, immunoglobulin chains or fragments thereof (such as Fv, Fab, Fab', F(ab')₂ or other antigen-binding subsequences of antibodies) that are principally comprised of the sequence of a human immunoglobulin, and contain minimal sequence derived from a non-human immunoglobulin. Humanization can be performed following the method of Winter and co-workers (Jones et al., Nature, 321:522-525 (1986); Riechmann et al., Nature, 332:323-327 (1988); Verhoeyen et al., Science, 239:1534-1536 (1988)), by substituting rodent CDRs or CDR sequences for the corresponding sequences of a human antibody. (See also U.S. Patent No. 5,225,539.) In some instances, Fv framework residues of the human immunoglobulin are replaced by corresponding non-human residues. Humanized antibodies can also comprise residues which are found neither in the recipient antibody nor in the

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imported CDR or framework sequences. In general, the humanized antibody will comprise substantially all of at least one, and typically two, variable domains, in which all or substantially all of the CDR regions correspond to those of a non-human immunoglobulin and all or substantially all of the framework regions are those of a human immunoglobulin consensus sequence. The humanized antibody optimally also will comprise at least a portion of an immunoglobulin constant region (Fc), typically that of a human immunoglobulin (Jones et al., 1986; Riechmann et al., 1988; and Presta, Curr. Op. Struct. Biol., 2:593-596 (1992)).

4.13.4 HUMAN ANTIBODIES

Fully human antibodies relate to antibody molecules in which essentially the entire sequences of both the light chain and the heavy chain, including the CDRs, arise from human genes. Such antibodies are termed "human antibodies", or "fully human antibodies" herein. Human monoclonal antibodies can be prepared by the trioma technique; the human B-cell hybridoma technique (see Kozbor, et al., 1983 Immunol Today 4: 72) and the EBV hybridoma technique to produce human monoclonal antibodies (see Cole, et al., 1985 In: MONOCLONAL ANTIBODIES AND CANCER THERAPY, Alan R. Liss, Inc., pp. 77-96). Human monoclonal antibodies may be utilized in the practice of the present invention and may be produced by using human hybridomas (see Cote, et al., 1983. Proc Natl Acad Sci USA 80: 2026-2030) or by transforming human B-cells with Epstein Barr Virus in vitro (see Cole, et al., 1985 In: MONOCLONAL ANTIBODIES AND CANCER THERAPY, Alan R. Liss, Inc., pp. 77-96).

In addition, human antibodies can also be produced using additional techniques, including phage display libraries (Hoogenboom and Winter, <u>J. Mol. Biol.</u>, <u>227</u>:381 (1991); Marks et al., <u>J. Mol. Biol.</u>, <u>222</u>:581 (1991)). Similarly, human antibodies can be made by introducing human immunoglobulin loci into transgenic animals, e.g., mice in which the endogenous immunoglobulin genes have been partially or completely inactivated. Upon challenge, human antibody production is observed, which closely resembles that seen in humans in all respects, including gene rearrangement, assembly, and antibody repertoire. This approach is described, for example, in U.S. Patent Nos. 5,545,807; 5,545,806; 5,569,825; 5,625,126; 5,633,425; 5,661,016, and in Marks et al. (<u>Bio/Technology 10</u>, 779-783 (1992)); Lonberg et al. (<u>Nature 368</u> 856-859 (1994)); Morrison (<u>Nature 368</u>, 812-13 (1994)); Fishwild et al. (<u>Nature Biotechnology 14</u>, 845-51 (1996)); Neuberger (Nature

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<u>Biotechnology</u> 14, 826 (1996)); and Lonberg and Huszar (<u>Intern. Rev. Immunol.</u> 13 65-93 (1995)).

Human antibodies may additionally be produced using transgenic nonhuman animals which are modified so as to produce fully human antibodies rather than the animal's endogenous antibodies in response to challenge by an antigen. (See PCT publication WO94/02602). The endogenous genes encoding the heavy and light immunoglobulin chains in the nonhuman host have been incapacitated, and active loci encoding human heavy and light chain immunoglobulins are inserted into the host's genome. The human genes are incorporated, for example, using yeast artificial chromosomes containing the requisite human DNA segments. An animal which provides all the desired modifications is then obtained as progeny by crossbreeding intermediate transgenic animals containing fewer than the full complement of the modifications. The preferred embodiment of such a nonhuman animal is a mouse, and is termed the XenomouseTM as disclosed in PCT publications WO 96/33735 and WO 96/34096. This animal produces B cells which secrete fully human immunoglobulins. The antibodies can be obtained directly from the animal after immunization with an immunogen of interest, as, for example, a preparation of a polyclonal antibody, or alternatively from immortalized B cells derived from the animal, such as hybridomas producing monoclonal antibodies. Additionally, the genes encoding the immunoglobulins with human variable regions can be recovered and expressed to obtain the antibodies directly, or can be further modified to obtain analogs of antibodies such as, for example, single chain Fv molecules.

An example of a method of producing a nonhuman host, exemplified as a mouse, lacking expression of an endogenous immunoglobulin heavy chain is disclosed in U.S. Patent No. 5,939,598. It can be obtained by a method including deleting the J segment genes from at least one endogenous heavy chain locus in an embryonic stem cell to prevent rearrangement of the locus and to prevent formation of a transcript of a rearranged immunoglobulin heavy chain locus, the deletion being effected by a targeting vector containing a gene encoding a selectable marker; and producing from the embryonic stem cell a transgenic mouse whose somatic and germ cells contain the gene encoding the selectable marker.

A method for producing an antibody of interest, such as a human antibody, is disclosed in U.S. Patent No. 5,916,771. It includes introducing an expression vector that contains a nucleotide sequence encoding a heavy chain into one mammalian host cell in

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culture, introducing an expression vector containing a nucleotide sequence encoding a light chain into another mammalian host cell, and fusing the two cells to form a hybrid cell. The hybrid cell expresses an antibody containing the heavy chain and the light chain.

In a further improvement on this procedure, a method for identifying a clinically relevant epitope on an immunogen, and a correlative method for selecting an antibody that binds immunospecifically to the relevant epitope with high affinity, are disclosed in PCT publication WO 99/53049.

4.13.5 Fab FRAGMENTS AND SINGLE CHAIN ANTIBODIES

According to the invention, techniques can be adapted for the production of single-chain antibodies specific to an antigenic protein of the invention (see e.g., U.S. Patent No. 4,946,778). In addition, methods can be adapted for the construction of F_{ab} expression libraries (see e.g., Huse, et al., 1989 Science 246: 1275-1281) to allow rapid and effective identification of monoclonal F_{ab} fragments with the desired specificity for a protein or derivatives, fragments, analogs or homologs thereof. Antibody fragments that contain the idiotypes to a protein antigen may be produced by techniques known in the art including, but not limited to: (i) an $F_{(ab)2}$ fragment produced by pepsin digestion of an antibody molecule; (ii) an F_{ab} fragment generated by reducing the disulfide bridges of an $F_{(ab)2}$ fragment; (iii) an F_{ab} fragment generated by the treatment of the antibody molecule with papain and a reducing agent and (iv) F_{v} fragments.

4.13.6 BISPECIFIC ANTIBODIES

Bispecific antibodies are monoclonal, preferably human or humanized, antibodies that have binding specificities for at least two different antigens. In the present case, one of the binding specificities is for an antigenic protein of the invention. The second binding target is any other antigen, and advantageously is a cell-surface protein or receptor or receptor subunit.

Methods for making bispecific antibodies are known in the art. Traditionally, the recombinant production of bispecific antibodies is based on the co-expression of two immunoglobulin heavy-chain/light-chain pairs, where the two heavy chains have different specificities (Milstein and Cuello, Nature, 305:537-539 (1983)). Because of the random assortment of immunoglobulin heavy and light chains, these hybridomas (quadromas) produce a potential mixture of ten different antibody molecules, of which only one has the

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correct bispecific structure. The purification of the correct molecule is usually accomplished by affinity chromatography steps. Similar procedures are disclosed in WO 93/08829, published 13 May 1993, and in Traunecker *et al.*, 1991 *EMBO J.*, 10:3655-3659.

Antibody variable domains with the desired binding specificities (antibody-antigen combining sites) can be fused to immunoglobulin constant domain sequences. The fusion preferably is with an immunoglobulin heavy-chain constant domain, comprising at least part of the hinge, CH2, and CH3 regions. It is preferred to have the first heavy-chain constant region (CH1) containing the site necessary for light-chain binding present in at least one of the fusions. DNAs encoding the immunoglobulin heavy-chain fusions and, if desired, the immunoglobulin light chain, are inserted into separate expression vectors, and are cotransfected into a suitable host organism. For further details of generating bispecific antibodies see, for example, Suresh et al., Methods in Enzymology, 121:210 (1986).

According to another approach described in WO 96/27011, the interface between a pair of antibody molecules can be engineered to maximize the percentage of heterodimers which are recovered from recombinant cell culture. The preferred interface comprises at least a part of the CH3 region of an antibody constant domain. In this method, one or more small amino acid side chains from the interface of the first antibody molecule are replaced with larger side chains (e.g. tyrosine or tryptophan). Compensatory "cavities" of identical or similar size to the large side chain(s) are created on the interface of the second antibody molecule by replacing large amino acid side chains with smaller ones (e.g. alanine or threonine). This provides a mechanism for increasing the yield of the heterodimer over other unwanted end-products such as homodimers.

Bispecific antibodies can be prepared as full length antibodies or antibody fragments (e.g. F(ab')₂ bispecific antibodies). Techniques for generating bispecific antibodies from antibody fragments have been described in the literature. For example, bispecific antibodies can be prepared using chemical linkage. Brennan et al., Science 229:81 (1985) describe a procedure wherein intact antibodies are proteolytically cleaved to generate F(ab')₂ fragments. These fragments are reduced in the presence of the dithiol complexing agent sodium arsenite to stabilize vicinal dithiols and prevent intermolecular disulfide formation. The Fab' fragments generated are then converted to thionitrobenzoate (TNB) derivatives. One of the Fab'-TNB derivatives is then reconverted to the Fab'-thiol by reduction with mercaptoethylamine and is mixed with an equimolar amount of the other Fab'-TNB

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derivative to form the bispecific antibody. The bispecific antibodies produced can be used as agents for the selective immobilization of enzymes.

Additionally, Fab' fragments can be directly recovered from E. coli and chemically coupled to form bispecific antibodies. Shalaby et al., J. Exp. Med. 175:217-225 (1992) describe the production of a fully humanized bispecific antibody F(ab')₂ molecule. Each Fab' fragment was separately secreted from E. coli and subjected to directed chemical coupling in vitro to form the bispecific antibody. The bispecific antibody thus formed was able to bind to cells overexpressing the ErbB2 receptor and normal human T cells, as well as trigger the lytic activity of human cytotoxic lymphocytes against human breast tumor targets.

Various techniques for making and isolating bispecific antibody fragments directly from recombinant cell culture have also been described. For example, bispecific antibodies have been produced using leucine zippers. Kostelny et al., J. Immunol. 148(5):1547-1553 (1992). The leucine zipper peptides from the Fos and Jun proteins were linked to the Fab' portions of two different antibodies by gene fusion. The antibody homodimers were reduced at the hinge region to form monomers and then re-oxidized to form the antibody heterodimers. This method can also be utilized for the production of antibody homodimers. The "diabody" technology described by Hollinger et al., Proc. Natl. Acad. Sci. USA 90:6444-6448 (1993) has provided an alternative mechanism for making bispecific antibody fragments. The fragments comprise a heavy-chain variable domain (VH) connected to a light-chain variable domain (V_L) by a linker which is too short to allow pairing between the two domains on the same chain. Accordingly, the V_H and V_L domains of one fragment are forced to pair with the complementary V_L and V_H domains of another fragment, thereby forming two antigen-binding sites. Another strategy for making bispecific antibody fragments by the use of single-chain Fv (sFv) dimers has also been reported. See, Gruber et al., J. Immunol. 152:5368 (1994).

Antibodies with more than two valencies are contemplated. For example, trispecific antibodies can be prepared. Tutt et al., <u>J. Immunol.</u> 147:60 (1991). Exemplary bispecific antibodies can bind to two different epitopes, at least one of which originates in the protein antigen of the invention. Alternatively, an anti-antigenic arm of an immunoglobulin molecule can be combined with an arm which binds to a triggering molecule on a leukocyte such as a T-cell receptor molecule (e.g. CD2, CD3, CD28, or B7), or Fc receptors for IgG (FcyR), such as FcyRI (CD64), FcyRII (CD32) and FcyRII (CD16) so as to focus cellular defense mechanisms to the cell expressing the particular antigen. Bispecific

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antibodies can also be used to direct cytotoxic agents to cells which express a particular antigen. These antibodies possess an antigen-binding arm and an arm which binds a cytotoxic agent or a radionuclide chelator, such as EOTUBE, DPTA, DOTA, or TETA. Another bispecific antibody of interest binds the protein antigen described herein and further binds tissue factor (TF).

4.13.7 HETEROCONJUGATE ANTIBODIES

Heteroconjugate antibodies are also within the scope of the present invention. Heteroconjugate antibodies are composed of two covalently joined antibodies. Such antibodies have, for example, been proposed to target immune system cells to unwanted cells (U.S. Patent No. 4,676,980), and for treatment of HIV infection (WO 91/00360; WO 92/200373; EP 03089). It is contemplated that the antibodies can be prepared in vitro using known methods in synthetic protein chemistry, including those involving crosslinking agents. For example, immunotoxins can be constructed using a disulfide exchange reaction or by forming a thioether bond. Examples of suitable reagents for this purpose include iminothiolate and methyl-4-mercaptobutyrimidate and those disclosed, for example, in U.S. Patent No. 4,676,980.

4.13.8 EFFECTOR FUNCTION ENGINEERING

It can be desirable to modify the antibody of the invention with respect to effector function, so as to enhance, e.g., the effectiveness of the antibody in treating cancer. For example, cysteine residue(s) can be introduced into the Fc region, thereby allowing interchain disulfide bond formation in this region. The homodimeric antibody thus generated can have improved internalization capability and/or increased complement-mediated cell killing and antibody-dependent cellular cytotoxicity (ADCC). See Caron et al., J. Exp Med., 176: 1191-1195 (1992) and Shopes, J. Immunol., 148: 2918-2922 (1992). Homodimeric antibodies with enhanced anti-tumor activity can also be prepared using heterobifunctional cross-linkers as described in Wolff et al. Cancer Research, 53: 2560-2565 (1993). Alternatively, an antibody can be engineered that has dual Fc regions and can thereby have enhanced complement lysis and ADCC capabilities. See Stevenson et al., Anti-Cancer Drug Design, 3: 219-230 (1989).

4.13.9 IMMUNOCONJUGATES

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The invention also pertains to immunoconjugates comprising an antibody conjugated to a cytotoxic agent such as a chemotherapeutic agent, toxin (e.g., an enzymatically active toxin of bacterial, fungal, plant, or animal origin, or fragments thereof), or a radioactive isotope (i.e., a radioconjugate).

Chemotherapeutic agents useful in the generation of such immunoconjugates have been described above. Enzymatically active toxins and fragments thereof that can be used include diphtheria A chain, nonbinding active fragments of diphtheria toxin, exotoxin A chain (from Pseudomonas aeruginosa), ricin A chain, abrin A chain, modeccin A chain, alpha-sarcin, Aleurites fordii proteins, dianthin proteins, Phytolaca americana proteins (PAPI, PAPII, and PAP-S), momordica charantia inhibitor, curcin, crotin, sapaonaria officinalis inhibitor, gelonin, mitogellin, restrictocin, phenomycin, enomycin, and the tricothecenes. A variety of radionuclides are available for the production of radioconjugated antibodies. Examples include ²¹²Bi, ¹³¹I, ¹³¹In, ⁹⁰Y, and ¹⁸⁶Re.

Conjugates of the antibody and cytotoxic agent are made using a variety of bifunctional protein-coupling agents such as N-succinimidyl-3-(2-pyridyldithiol) propionate (SPDP), iminothiolane (IT), bifunctional derivatives of imidoesters (such as dimethyl adipimidate HCL), active esters (such as disuccinimidyl suberate), aldehydes (such as glutareldehyde), bis-azido compounds (such as bis (p-azidobenzoyl) hexanediamine), bis-diazonium derivatives (such as bis-(p-diazoniumbenzoyl)-ethylenediamine), diisocyanates (such as tolyene 2,6-diisocyanate), and bis-active fluorine compounds (such as 1,5-difluoro-2,4-dinitrobenzene). For example, a ricin immunotoxin can be prepared as described in Vitetta et al., Science, 238: 1098 (1987). Carbon-14-labeled 1-isothiocyanatobenzyl-3-methyldiethylene triaminepentaacetic acid (MX-DTPA) is an exemplary chelating agent for conjugation of radionucleotide to the antibody. See WO94/11026.

In another embodiment, the antibody can be conjugated to a "receptor" (such as streptavidin) for utilization in tumor pretargeting wherein the antibody-receptor conjugate is administered to the patient, followed by removal of unbound conjugate from the circulation using a clearing agent and then administration of a "ligand" (e.g., avidin) that is in turn conjugated to a cytotoxic agent.

4.14 COMPUTER READABLE SEQUENCES

In one application of this embodiment, a nucleotide sequence of the present invention can be recorded on computer readable media. As used herein, "computer readable media"

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refers to any medium which can be read and accessed directly by a computer. Such media include, but are not limited to: magnetic storage media, such as floppy discs, hard disc storage medium, and magnetic tape; optical storage media such as CD-ROM; electrical storage media such as RAM and ROM; and hybrids of these categories such as magnetic/optical storage media. A skilled artisan can readily appreciate how any of the presently known computer readable mediums can be used to create a manufacture comprising computer readable medium having recorded thereon a nucleotide sequence of the present invention. As used herein, "recorded" refers to a process for storing information on computer readable medium. A skilled artisan can readily adopt any of the presently known methods for recording information on computer readable medium to generate manufactures comprising the nucleotide sequence information of the present invention.

A variety of data storage structures are available to a skilled artisan for creating a computer readable medium having recorded thereon a nucleotide sequence of the present invention. The choice of the data storage structure will generally be based on the means chosen to access the stored information. In addition, a variety of data processor programs and formats can be used to store the nucleotide sequence information of the present invention on computer readable medium. The sequence information can be represented in a word processing text file, formatted in commercially-available software such as WordPerfect and Microsoft Word, or represented in the form of an ASCII file, stored in a database application, such as DB2, Sybase, Oracle, or the like. A skilled artisan can readily adapt any number of data processor structuring formats (e.g. text file or database) in order to obtain computer readable medium having recorded thereon the nucleotide sequence information of the present invention.

By providing any of the nucleotide sequences SEQ ID NO: 1-93 or a representative fragment thereof; or a nucleotide sequence at least 95% identical to any of the nucleotide sequences of SEQ ID NO: 1-93 in computer readable form, a skilled artisan can routinely access the sequence information for a variety of purposes. Computer software is publicly available which allows a skilled artisan to access sequence information provided in a computer readable medium. The examples which follow demonstrate how software which implements the BLAST (Altschul et al., J. Mol. Biol. 215:403-410 (1990)) and BLAZE (Brutlag et al., Comp. Chem. 17:203-207 (1993)) search algorithms on a Sybase system is used to identify open reading frames (ORFs) within a nucleic acid sequence. Such ORFs may be protein encoding fragments and may be useful in producing commercially important

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proteins such as enzymes used in fermentation reactions and in the production of commercially useful metabolites.

As used herein, "a computer-based system" refers to the hardware means, software means, and data storage means used to analyze the nucleotide sequence information of the present invention. The minimum hardware means of the computer-based systems of the present invention comprises a central processing unit (CPU), input means, output means, and data storage means. A skilled artisan can readily appreciate that any one of the currently available computer-based systems are suitable for use in the present invention. As stated above, the computer-based systems of the present invention comprise a data storage means having stored therein a nucleotide sequence of the present invention and the necessary hardware means and software means for supporting and implementing a search means. As used herein, "data storage means" refers to memory which can store nucleotide sequence information of the present invention, or a memory access means which can access manufactures having recorded thereon the nucleotide sequence information of the present invention.

As used herein, "search means" refers to one or more programs which are implemented on the computer-based system to compare a target sequence or target structural motif with the sequence information stored within the data storage means. Search means are used to identify fragments or regions of a known sequence which match a particular target sequence or target motif. A variety of known algorithms are disclosed publicly and a variety of commercially available software for conducting search means are and can be used in the computer-based systems of the present invention. Examples of such software includes, but is not limited to, Smith-Waterman, MacPattern (EMBL), BLASTN and BLASTA (NPOLYPEPTIDEIA). A skilled artisan can readily recognize that any one of the available algorithms or implementing software packages for conducting homology searches can be adapted for use in the present computer-based systems. As used herein, a "target sequence" can be any nucleic acid or amino acid sequence of six or more nucleotides or two or more amino acids. A skilled artisan can readily recognize that the longer a target sequence is, the less likely a target sequence will be present as a random occurrence in the database. The most preferred sequence length of a target sequence is from about 10 to 300 amino acids, more preferably from about 30 to 100 nucleotide residues. However, it is well recognized that searches for commercially important fragments, such as sequence fragments involved in gene expression and protein processing, may be of shorter length.

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As used herein, "a target structural motif," or "target motif," refers to any rationally selected sequence or combination of sequences in which the sequence(s) are chosen based on a three-dimensional configuration which is formed upon the folding of the target motif.

There are a variety of target motifs known in the art. Protein target motifs include, but are not limited to, enzyme active sites and signal sequences. Nucleic acid target motifs include, but are not limited to, promoter sequences, hairpin structures and inducible expression elements (protein binding sequences).

4.15 TRIPLE HELIX FORMATION

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In addition, the fragments of the present invention, as broadly described, can be used to control gene expression through triple helix formation or antisense DNA or RNA, both of which methods are based on the binding of a polynucleotide sequence to DNA or RNA. Polynucleotides suitable for use in these methods are preferably 20 to 40 bases in length and are designed to be complementary to a region of the gene involved in transcription (triple helix - see Lee et al., Nucl. Acids Res. 6:3073 (1979); Cooney et al., Science 15241:456 (1988); and Dervan et al., Science 251:1360 (1991)) or to the mRNA itself (antisense - Olmno, J. Neurochem. 56:560 (1991); Oligodeoxynucleotides as Antisense Inhibitors of Gene Expression, CRC Press, Boca Raton, FL (1988)). Triple helix-formation optimally results in a shut-off of RNA transcription from DNA, while antisense RNA hybridization blocks translation of an mRNA molecule into polypeptide. Both techniques have been demonstrated to be effective in model systems. Information contained in the sequences of the present invention is necessary for the design of an antisense or triple helix oligonucleotide.

4.16 DIAGNOSTIC ASSAYS AND KITS

The present invention further provides methods to identify the presence or expression of one of the ORFs of the present invention, or homolog thereof, in a test sample, using a nucleic acid probe or antibodies of the present invention, optionally conjugated or otherwise associated with a suitable label.

In general, methods for detecting a polynucleotide of the invention can comprise contacting a sample with a compound that binds to and forms a complex with the polynucleotide for a period sufficient to form the complex, and detecting the complex, so that if a complex is detected, a polynucleotide of the invention is detected in the sample. Such methods can also comprise contacting a sample under stringent hybridization conditions with

nucleic acid primers that anneal to a polynucleotide of the invention under such conditions, and amplifying annealed polynucleotides, so that if a polynucleotide is amplified, a polynucleotide of the invention is detected in the sample.

In general, methods for detecting a polypeptide of the invention can comprise contacting a sample with a compound that binds to and forms a complex with the polypeptide for a period sufficient to form the complex, and detecting the complex, so that if a complex is detected, a polypeptide of the invention is detected in the sample.

In detail, such methods comprise incubating a test sample with one or more of the antibodies or one or more of the nucleic acid probes of the present invention and assaying for binding of the nucleic acid probes or antibodies to components within the test sample.

Conditions for incubating a nucleic acid probe or antibody with a test sample vary. Incubation conditions depend on the format employed in the assay, the detection methods employed, and the type and nature of the nucleic acid probe or antibody used in the assay. One skilled in the art will recognize that any one of the commonly available hybridization, amplification or immunological assay formats can readily be adapted to employ the nucleic acid probes or antibodies of the present invention. Examples of such assays can be found in Chard, T., An Introduction to Radioimmunoassay and Related Techniques, Elsevier Science Publishers, Amsterdam, The Netherlands (1986); Bullock, G.R. et al., Techniques in Immunocytochemistry, Academic Press, Orlando, FL Vol. 1 (1982), Vol. 2 (1983), Vol. 3 (1985); Tijssen, P., Practice and Theory of immunoassays: Laboratory Techniques in Biochemistry and Molecular Biology, Elsevier Science Publishers, Amsterdam, The Netherlands (1985). The test samples of the present invention include cells, protein or membrane extracts of cells, or biological fluids such as sputum, blood, serum, plasma, or urine. The test sample used in the above-described method will vary based on the assay format, nature of the detection method and the tissues, cells or extracts used as the sample to be assayed. Methods for preparing protein extracts or membrane extracts of cells are well known in the art and can be readily be adapted in order to obtain a sample which is compatible with the system utilized.

In another embodiment of the present invention, kits are provided which contain the necessary reagents to carry out the assays of the present invention. Specifically, the invention provides a compartment kit to receive, in close confinement, one or more containers which comprises: (a) a first container comprising one of the probes or antibodies of the present invention; and (b) one or more other containers comprising one or more of the

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following: wash reagents, reagents capable of detecting presence of a bound probe or antibody.

In detail, a compartment kit includes any kit in which reagents are contained in separate containers. Such containers include small glass containers, plastic containers or strips of plastic or paper. Such containers allows one to efficiently transfer reagents from one compartment to another compartment such that the samples and reagents are not cross-contaminated, and the agents or solutions of each container can be added in a quantitative fashion from one compartment to another. Such containers will include a container which will accept the test sample, a container which contains the antibodies used in the assay, containers which contain wash reagents (such as phosphate buffered saline, Tris-buffers, etc.), and containers which contain the reagents used to detect the bound antibody or probe. Types of detection reagents include labeled nucleic acid probes, labeled secondary antibodies, or in the alternative, if the primary antibody is labeled, the enzymatic, or antibody binding reagents which are capable of reacting with the labeled antibody. One skilled in the art will readily recognize that the disclosed probes and antibodies of the present invention can be readily incorporated into one of the established kit formats which are well known in the art.

4.17 MEDICAL IMAGING

The novel polypeptides and binding partners of the invention are useful in medical imaging of sites expressing the molecules of the invention (e.g., where the polypeptide of the invention is involved in the immune response, for imaging sites of inflammation or infection). See, e.g., Kunkel et al., U.S. Pat. NO. 5,413,778. Such methods involve chemical attachment of a labeling or imaging agent, administration of the labeled polypeptide to a subject in a pharmaceutically acceptable carrier, and imaging the labeled polypeptide *in vivo* at the target site.

4.18 SCREENING ASSAYS

Using the isolated proteins and polynucleotides of the invention, the present invention further provides methods of obtaining and identifying agents which bind to a polypeptide encoded by an ORF corresponding to any of the nucleotide sequences set forth in SEQ ID NO: 1-93, or bind to a specific domain of the polypeptide encoded by the nucleic acid. In detail, said method comprises the steps of:

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(a) contacting an agent with an isolated protein encoded by an ORF of the present invention, or nucleic acid of the invention; and

(b) determining whether the agent binds to said protein or said nucleic acid.

In general, therefore, such methods for identifying compounds that bind to a polynucleotide of the invention can comprise contacting a compound with a polynucleotide of the invention for a time sufficient to form a polynucleotide/compound complex, and detecting the complex, so that if a polynucleotide/compound complex is detected, a compound that binds to a polynucleotide of the invention is identified.

Likewise, in general, therefore, such methods for identifying compounds that bind to a polypeptide of the invention can comprise contacting a compound with a polypeptide of the invention for a time sufficient to form a polypeptide/compound complex, and detecting the complex, so that if a polypeptide/compound complex is detected, a compound that binds to a polynucleotide of the invention is identified.

Methods for identifying compounds that bind to a polypeptide of the invention can also comprise contacting a compound with a polypeptide of the invention in a cell for a time sufficient to form a polypeptide/compound complex, wherein the complex drives expression of a receptor gene sequence in the cell, and detecting the complex by detecting reporter gene sequence expression, so that if a polypeptide/compound complex is detected, a compound that binds a polypeptide of the invention is identified.

Compounds identified via such methods can include compounds which modulate the activity of a polypeptide of the invention (that is, increase or decrease its activity, relative to activity observed in the absence of the compound). Alternatively, compounds identified via such methods can include compounds which modulate the expression of a polynucleotide of the invention (that is, increase or decrease expression relative to expression levels observed in the absence of the compound). Compounds, such as compounds identified via the methods of the invention, can be tested using standard assays well known to those of skill in the art for their ability to modulate activity/expression.

The agents screened in the above assay can be, but are not limited to, peptides, carbohydrates, vitamin derivatives, or other pharmaceutical agents. The agents can be selected and screened at random or rationally selected or designed using protein modeling techniques.

For random screening, agents such as peptides, carbohydrates, pharmaceutical agents and the like are selected at random and are assayed for their ability to bind to the protein

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encoded by the ORF of the present invention. Alternatively, agents may be rationally selected or designed. As used herein, an agent is said to be "rationally selected or designed" when the agent is chosen based on the configuration of the particular protein. For example, one skilled in the art can readily adapt currently available procedures to generate peptides, pharmaceutical agents and the like, capable of binding to a specific peptide sequence, in order to generate rationally designed antipeptide peptides, for example see Hurby et al., Application of Synthetic Peptides: Antisense Peptides," In Synthetic Peptides, A User's Guide, W.H. Freeman, NY (1992), pp. 289-307, and Kaspczak et al., Biochemistry 28:9230-8 (1989), or pharmaceutical agents, or the like.

In addition to the foregoing, one class of agents of the present invention, as broadly described, can be used to control gene expression through binding to one of the ORFs or EMFs of the present invention. As described above, such agents can be randomly screened or rationally designed/selected. Targeting the ORF or EMF allows a skilled artisan to design sequence specific or element specific agents, modulating the expression of either a single ORF or multiple ORFs which rely on the same EMF for expression control. One class of DNA binding agents are agents which contain base residues which hybridize or form a triple helix formation by binding to DNA or RNA. Such agents can be based on the classic phosphodiester, ribonucleic acid backbone, or can be a variety of sulfhydryl or polymeric derivatives which have base attachment capacity.

Agents suitable for use in these methods preferably contain 20 to 40 bases and are designed to be complementary to a region of the gene involved in transcription (triple helix - see Lee et al., Nucl. Acids Res. 6:3073 (1979); Cooney et al., Science 241:456 (1988); and Dervan et al., Science 251:1360 (1991)) or to the mRNA itself (antisense - Okano, J. Neurochem. 56:560 (1991); Oligodeoxynucleotides as Antisense Inhibitors of Gene Expression, CRC Press, Boca Raton, FL (1988)). Triple helix-formation optimally results in a shut-off of RNA transcription from DNA, while antisense RNA hybridization blocks translation of an mRNA molecule into polypeptide. Both techniques have been demonstrated to be effective in model systems. Information contained in the sequences of the present invention is necessary for the design of an antisense or triple helix oligonucleotide and other DNA binding agents.

Agents which bind to a protein encoded by one of the ORFs of the present invention can be used as a diagnostic agent. Agents which bind to a protein encoded by one of the

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ORFs of the present invention can be formulated using known techniques to generate a pharmaceutical composition.

4.19 USE OF NUCLEIC ACIDS AS PROBES

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Another aspect of the subject invention is to provide for polypeptide-specific nucleic acid hybridization probes capable of hybridizing with naturally occurring nucleotide sequences. The hybridization probes of the subject invention may be derived from any of the nucleotide sequences SEQ ID NO: 1-93. Because the corresponding gene is only expressed in a limited number of tissues, a hybridization probe derived from any of the nucleotide sequences SEQ ID NO: 1-93 can be used as an indicator of the presence of RNA of cell type of such a tissue in a sample.

Any suitable hybridization technique can be employed, such as, for example, in situ hybridization. PCR as described in US Patents Nos. 4,683,195 and 4,965,188 provides additional uses for oligonucleotides based upon the nucleotide sequences. Such probes used in PCR may be of recombinant origin, may be chemically synthesized, or a mixture of both. The probe will comprise a discrete nucleotide sequence for the detection of identical sequences or a degenerate pool of possible sequences for identification of closely related genomic sequences.

Other means for producing specific hybridization probes for nucleic acids include the cloning of nucleic acid sequences into vectors for the production of mRNA probes. Such vectors are known in the art and are commercially available and may be used to synthesize RNA probes in vitro by means of the addition of the appropriate RNA polymerase as T7 or SP6 RNA polymerase and the appropriate radioactively labeled nucleotides. The nucleotide sequences may be used to construct hybridization probes for mapping their respective genomic sequences. The nucleotide sequence provided herein may be mapped to a chromosome or specific regions of a chromosome using well known genetic and/or chromosomal mapping techniques. These techniques include in situ hybridization, linkage analysis against known chromosomal markers, hybridization screening with libraries or flow-sorted chromosomal preparations specific to known chromosomes, and the like. The technique of fluorescent in situ hybridization of chromosome spreads has been described, among other places, in Verma et al (1988) Human Chromosomes: A Manual of Basic Techniques, Pergamon Press, New York NY.

Fluorescent in situ hybridization of chromosomal preparations and other physical chromosome mapping techniques may be correlated with additional genetic map data. Examples of genetic map data can be found in the 1994 Genome Issue of Science (265:1981f). Correlation between the location of a nucleic acid on a physical chromosomal map and a specific disease (or predisposition to a specific disease) may help delimit the region of DNA associated with that genetic disease. The nucleotide sequences of the subject invention may be used to detect differences in gene sequences between normal, carrier or affected individuals.

4.20 PREPARATION OF SUPPORT BOUND OLIGONUCLEOTIDES

Oligonucleotides, i.e., small nucleic acid segments, may be readily prepared by, for example, directly synthesizing the oligonucleotide by chemical means, as is commonly practiced using an automated oligonucleotide synthesizer.

Support bound oligonucleotides may be prepared by any of the methods known to those of skill in the art using any suitable support such as glass, polystyrene or Teflon. One strategy is to precisely spot oligonucleotides synthesized by standard synthesizers. Immobilization can be achieved using passive adsorption (Inouye & Hondo, (1990) J. Clin. Microbiol. 28(6) 1469-72); using UV light (Nagata et al., 1985; Dahlen et al., 1987; Morrissey & Collins, (1989) Mol. Cell Probes 3(2) 189-207) or by covalent binding of base modified DNA (Keller et al., 1988; 1989); all references being specifically incorporated herein.

Another strategy that may be employed is the use of the strong biotin-streptavidin interaction as a linker. For example, Broude *et al.* (1994) Proc. Natl. Acad. Sci. USA 91(8) 3072-6, describe the use of biotinylated probes, although these are duplex probes, that are immobilized on streptavidin-coated magnetic beads. Streptavidin-coated beads may be purchased from Dynal, Oslo. Of course, this same linking chemistry is applicable to coating any surface with streptavidin. Biotinylated probes may be purchased from various sources, such as, e.g., Operon Technologies (Alameda, CA).

Nunc Laboratories (Naperville, IL) is also selling suitable material that could be used.

Nunc Laboratories have developed a method by which DNA can be covalently bound to the microwell surface termed Covalink NH. CovaLink NH is a polystyrene surface grafted with secondary amino groups (>NH) that serve as bridge-heads for further covalent coupling.

CovaLink Modules may be purchased from Nunc Laboratories. DNA molecules may be bound

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to CovaLink exclusively at the 5'-end by a phosphoramidate bond, allowing immobilization of more than 1 pmol of DNA (Rasmussen *et al.*, (1991) Anal. Biochem. 198(1) 138-42).

The use of CovaLink NH strips for covalent binding of DNA molecules at the 5'-end has been described (Rasmussen et al., (1991). In this technology, a phosphoramidate bond is employed (Chu et al., (1983) Nucleic Acids Res. 11(8) 6513-29). This is beneficial as immobilization using only a single covalent bond is preferred. The phosphoramidate bond joins the DNA to the CovaLink NH secondary amino groups that are positioned at the end of spacer arms covalently grafted onto the polystyrene surface through a 2 nm long spacer arm. To link an oligonucleotide to CovaLink NH via an phosphoramidate bond, the oligonucleotide terminus must have a 5'-end phosphate group. It is, perhaps, even possible for biotin to be covalently bound to CovaLink and then streptavidin used to bind the probes.

More specifically, the linkage method includes dissolving DNA in water (7.5 ng/μl) and denaturing for 10 min. at 95°C and cooling on ice for 10 min. Ice-cold 0.1 M 1-methylimidazole, pH 7.0 (1-MeIm₇), is then added to a final concentration of 10 mM 1-MeIm₇. The single-stranded DNA solution is then dispensed into CovaLink NH strips (75 μl/well) standing on ice.

Carbodiimide 0.2 M 1-ethyl-3-(3-dimethylaminopropyl)-carbodiimide (EDC), dissolved in 10 mM 1-MeIm₇, is made fresh and 25 µl added per well. The strips are incubated for 5 hours at 50°C. After incubation the strips are washed using, e.g., Nunc-Immuno Wash; first the wells are washed 3 times, then they are soaked with washing solution for 5 min., and finally they are washed 3 times (where in the washing solution is 0.4 N NaOH, 0.25% SDS heated to 50°C).

It is contemplated that a further suitable method for use with the present invention is that described in PCT Patent Application WO 90/03382 (Southern & Maskos), incorporated herein by reference. This method of preparing an oligonucleotide bound to a support involves attaching a nucleoside 3'-reagent through the phosphate group by a covalent phosphodiester link to aliphatic hydroxyl groups carried by the support. The oligonucleotide is then synthesized on the supported nucleoside and protecting groups removed from the synthetic oligonucleotide chain under standard conditions that do not cleave the oligonucleotide from the support. Suitable reagents include nucleoside phosphoramidite and nucleoside hydrogen phosphorate.

An on-chip strategy for the preparation of DNA probe for the preparation of DNA probe arrays may be employed. For example, addressable laser-activated photodeprotection may be employed in the chemical synthesis of oligonucleotides directly on a glass surface, as described by Fodor *et al.* (1991) Science 251(4995) 767-73, incorporated herein by reference. Probes may

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also be immobilized on nylon supports as described by Van Ness *et al.* (1991) Nucleic Acids Res. 19(12) 3345-50; or linked to Teflon using the method of Duncan & Cavalier (1988) Anal. Biochem. 169(1) 104-8; all references being specifically incorporated herein.

To link an oligonucleotide to a nylon support, as described by Van Ness *et al.* (1991), requires activation of the nylon surface via alkylation and selective activation of the 5'-amine of oligonucleotides with cyanuric chloride.

One particular way to prepare support bound oligonucleotides is to utilize the light-generated synthesis described by Pease *et al.*, (1994) PNAS USA 91(11) 5022-6, incorporated herein by reference). These authors used current photolithographic techniques to generate arrays of immobilized oligonucleotide probes (DNA chips). These methods, in which light is used to direct the synthesis of oligonucleotide probes in high-density, miniaturized arrays, utilize photolabile 5'-protected *N*-acyl-deoxynucleoside phosphoramidites, surface linker chemistry and versatile combinatorial synthesis strategies. A matrix of 256 spatially defined oligonucleotide probes may be generated in this manner.

4.21 PREPARATION OF NUCLEIC ACID FRAGMENTS

The nucleic acids may be obtained from any appropriate source, such as cDNAs, genomic DNA, chromosomal DNA, microdissected chromosome bands, cosmid or YAC inserts, and RNA, including mRNA without any amplification steps. For example, Sambrook *et al.* (1989) describes three protocols for the isolation of high molecular weight DNA from mammalian cells (p. 9.14-9.23).

DNA fragments may be prepared as clones in M13, plasmid or lambda vectors and/or prepared directly from genomic DNA or cDNA by PCR or other amplification methods. Samples may be prepared or dispensed in multiwell plates. About 100-1000 ng of DNA samples may be prepared in 2-500 ml of final volume.

The nucleic acids would then be fragmented by any of the methods known to those of skill in the art including, for example, using restriction enzymes as described at 9.24-9.28 of Sambrook *et al.* (1989), shearing by ultrasound and NaOH treatment.

Low pressure shearing is also appropriate, as described by Schriefer *et al.* (1990) Nucleic Acids Res. 18(24) 7455-6, incorporated herein by reference). In this method, DNA samples are passed through a small French pressure cell at a variety of low to intermediate pressures. A lever device allows controlled application of low to intermediate pressures to the cell. The

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results of these studies indicate that low-pressure shearing is a useful alternative to sonic and enzymatic DNA fragmentation methods.

One particularly suitable way for fragmenting DNA is contemplated to be that using the two base recognition endonuclease, *CviJI*, described by Fitzgerald *et al.* (1992) Nucleic Acids Res. 20(14) 3753-62. These authors described an approach for the rapid fragmentation and fractionation of DNA into particular sizes that they contemplated to be suitable for shotgun cloning and sequencing.

The restriction endonuclease $Cvi\Pi$ normally cleaves the recognition sequence PuGCPy between the G and C to leave blunt ends. Atypical reaction conditions, which alter the specificity of this enzyme ($Cvi\Pi^{**}$), yield a quasi-random distribution of DNA fragments form the small molecule pUC19 (2688 base pairs). Fitzgerald *et al.* (1992) quantitatively evaluated the randomness of this fragmentation strategy, using a $Cvi\Pi^{**}$ digest of pUC19 that was size fractionated by a rapid gel filtration method and directly ligated, without end repair, to a lac Z minus M13 cloning vector. Sequence analysis of 76 clones showed that $Cvi\Pi^{**}$ restricts pyGCPy and PuGCPu, in addition to PuGCPy sites, and that new sequence data is accumulated at a rate consistent with random fragmentation.

As reported in the literature, advantages of this approach compared to sonication and agarose gel fractionation include: smaller amounts of DNA are required (0.2-0.5 μ g instead of 2-5 μ g); and fewer steps are involved (no preligation, end repair, chemical extraction, or agarose gel electrophoresis and elution are needed

Irrespective of the manner in which the nucleic acid fragments are obtained or prepared, it is important to denature the DNA to give single stranded pieces available for hybridization. This is achieved by incubating the DNA solution for 2-5 minutes at 80-90°C. The solution is then cooled quickly to 2°C to prevent renaturation of the DNA fragments before they are contacted with the chip. Phosphate groups must also be removed from genomic DNA by methods known in the art.

4.22 PREPARATION OF DNA ARRAYS

Arrays may be prepared by spotting DNA samples on a support such as a nylon membrane. Spotting may be performed by using arrays of metal pins (the positions of which correspond to an array of wells in a microtiter plate) to repeated by transfer of about 20 nl of a DNA solution to a nylon membrane. By offset printing, a density of dots higher than the density of the wells is achieved. One to 25 dots may be accommodated in 1 mm², depending on the type

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of label used. By avoiding spotting in some preselected number of rows and columns, separate subsets (subarrays) may be formed. Samples in one subarray may be the same genomic segment of DNA (or the same gene) from different individuals, or may be different, overlapped genomic clones. Each of the subarrays may represent replica spotting of the same samples. In one example, a selected gene segment may be amplified from 64 patients. For each patient, the amplified gene segment may be in one 96-well plate (all 96 wells containing the same sample). A plate for each of the 64 patients is prepared. By using a 96-pin device, all samples may be spotted on one 8 x 12 cm membrane. Subarrays may contain 64 samples, one from each patient. Where the 96 subarrays are identical, the dot span may be 1 mm² and there may be a 1 mm space between subarrays.

Another approach is to use membranes or plates (available from NUNC, Naperville, Illinois) which may be partitioned by physical spacers e.g. a plastic grid molded over the membrane, the grid being similar to the sort of membrane applied to the bottom of multiwell plates, or hydrophobic strips. A fixed physical spacer is not preferred for imaging by exposure to flat phosphor-storage screens or x-ray films.

The present invention is illustrated in the following examples. Upon consideration of the present disclosure, one of skill in the art will appreciate that many other embodiments and variations may be made in the scope of the present invention. Accordingly, it is intended that the broader aspects of the present invention not be limited to the disclosure of the following examples. The present invention is not to be limited in scope by the exemplified embodiments which are intended as illustrations of single aspects of the invention, and compositions and methods which are functionally equivalent are within the scope of the invention. Indeed, numerous modifications and variations in the practice of the invention are expected to occur to those skilled in the art upon consideration of the present preferred embodiments. Consequently, the only limitations which should be placed upon the scope of the invention are those which appear in the appended claims.

All references cited within the body of the instant specification are hereby incorporated by reference in their entirety.

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5. EXAMPLES

5.1 EXAMPLE 1

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Novel Nucleic Acid Sequences Obtained From Various Libraries

A plurality of novel nucleic acids were obtained from cDNA libraries prepared from various human tissues and in some cases isolated from a genomic library derived from human chromosome using standard PCR, SBH sequence signature analysis and Sanger sequencing techniques. The inserts of the library were amplified with PCR using primers specific for the vector sequences which flank the inserts. Clones from cDNA libraries were spotted on nylon membrane filters and screened with oligonucleotide probes (e.g., 7-mers) to obtain signature sequences. The clones were clustered into groups of similar or identical sequences. Representative clones were selected for sequencing.

In some cases, the 5' sequence of the amplified inserts was then deduced using a typical Sanger sequencing protocol. PCR products were purified and subjected to fluorescent dye terminator cycle sequencing. Single pass gel sequencing was done using a 377 Applied Biosystems (ABI) sequencer to obtain the novel nucleic acid sequences

5.2 EXAMPLE 2

Assemblage of Novel Nucleic Acids

The nucleic acids of the present invention, designated as SEQ ID NO: 1-93 were assembled using an EST sequence as a seed. Then a recursive algorithm was used to extend the seed EST into an extended assemblage, by pulling additional sequences from different databases (i.e., Hyseq's database containing EST sequences, dbEST, gb pri, UniGene, and exons from public domain genomic sequences predicated by GenScan) that belong to this assemblage. The algorithm terminated when there was no additional sequences from the above databases that would extend the assemblage. Further, inclusion of component sequences into the assemblage was based on a BLASTN hit to the extending assemblage with BLAST score greater than 300 and percent identity greater than 95%.

Using PHRAP (Univ. of Washington) or CAP4 (Paracel), full-length gene sequences and their corresponding protein sequences were generated from the assemblage. Any frame shifts and incorrect stop codons were corrected by hand editing. During editing, the sequence was checked using FASTXY algorithm against Genbank (i.e., dbEST, gb pri, UniGene, and Genpept). Other computer programs which may have been used in the editing process were phredPhrap and Consed (University of Washington) and ed-ready, ed-ext and gc-zip-2 (Hyseq,

Inc.). The full-length nucleotide sequences are shown in the Sequence Listing as SEQ ID NO: 1-93. The corresponding polypeptide sequences are SEQ ID NO: 94-186.

Table 1 shows the various tissue sources of SEQ ID NO: 1-93.

The nearest neighbor results for polypeptides encoded by SEQ ID NO: 1-93 (i.e. SEQ ID NO: 94-186) were obtained by a BLASTP (version 2.0al 19MP-WashU) search against Genpept, Geneseq and SwissProt databases using BLAST algorithm. The nearest neighbor result showed the closest homologue with functional annotation for SEQ ID NO: 1-93. The translated amino acid sequences for which the nucleic acid sequence encodes are shown in the Sequence Listing. The homologues with identifiable functions for SEQ ID NO: 1-93 are shown in Table 2 below.

Using eMatrix software package (Stanford University, Stanford, CA) (Wu et al., J. Comp. Biol., Vol. 6 pp. 219-235 (1999) herein incorporated by reference), polypeptides encoded by SEQ ID NO: 1-93 (i.e. SEQ ID NO: 94-186) were examined to determine whether they had identifiable signature regions. Table 3 shows the signature region found in the indicated polypeptide sequences, the description of the signature, the eMatrix p-value(s) and the position(s) of the signature within the polypeptide sequence.

Using the Pfam software program (Sonnhammer et al., Nucleic Acids Res., Vol. 26(1) pp. 320-322 (1998) herein incorporated by reference) polypeptides encoded by SEQ ID NO: 1-93 (i.e. SEQ ID NO: 94-186) were examined for domains with homology to certain peptide domains. Table 4 shows the name of the domain found, the description, the product of all the e-value of similar domains found, the pFam score for the identified domain within the sequence, number of similar domains found, and the position of the domain in the SEQ ID NO: being interrorgated..

The GeneAtlas™ software package (Molecular Simulations Inc. (MSI), San Diego, CA) was used to predict the three-dimensional structure models for the polypeptides encoded by SEQ ID NO: 1-93 (i.e. SEQ ID NO: 94-186). Models were generated by (1) PSI-BLAST which is a multiple alignment sequence profile-based searching developed by Altschul et al, (Nucl. Acids. Res. 25, 3389-3408 (1997)), (2) High Throughput Modeling (HTM) (Molecular Simulations Inc. (MSI) San Diego, CA,) which is an automated sequence and structure searching procedure (http://www.msi.com/), and (3) SeqFold™ which is a fold recognition method described by Fischer and Eisenberg (J. Mol. Biol. 209, 779-791 (1998)). This analysis was carried out, in part, by comparing the polypeptides of the invention with the known NMR (nuclear magnetic resonance) and x-ray crystal three-dimensional structures as

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templates. Table 5 shows, "PDB ID", the Protein DataBase (PDB) identifier given to template structure; "Chain ID", identifier of the subcomponent of the PDB template structure; "Compound Information", information of the PDB template structure and/or its subcomponents; "PDB Function Annotation" gives function of the PDB template as annotated by the PDB files (http://www.rcsb.org/PDB/); start and end amino acid position of the protein sequence aligned; PSI-BLAST score, the verify score, the SeqFold score, and the Potential(s) of Mean Force (PMF). The verify score is produced by GeneAtlas™ software (MSI), is based on Dr. Eisenberg's Profile-3D threading program developed in Dr. David Eisenberg's laboratory (US patent no. 5,436,850 and Luthy, Bowie, and Eisenberg, Nature, 356:83-85 (1992)) and a publication by R. Sanchez and A. Sali, Proc. Natl. Acad. Sci. USA, 95:13597-12502. The verify score produced by GeneAtlas normalizes the verify score for proteins with different lengths so that a unified cutoff can be used to select good models as follows:

Verify score (normalized) = (raw score - 1/2 high score)/(1/2 high score)

The PFM score, produced by GeneAtlas[™] software (MSI), is a composite scoring function that depends in part on the compactness of the model, sequence identity in the alignment used to build the model, pairwise and surface mean force potentials (MFP). As given in Table 5, a verify score between 0 to 1.0, with 1 being the best, represents a good model. Similarly, a PMF score between 0 to 1.0, with 1 being the best, represents a good model. A SeqFold[™] score of more than 50 is considered significant. A good model may also be determined by one of skill in the art based all the information in Table 5 taken in totality.

The nucleotide sequence within the sequences that codes for signal peptide sequences and their cleavage sites can be determined from using Neural Network SignalP V1.1 program (from Center for Biological Sequence Analysis, The Technical University of Denmark). The process for identifying prokaryotic and eukaryotic signal peptides and their cleavage sites are also disclosed by Henrik Nielson, Jacob Engelbrecht, Soren Brunak, and Gunnar von Heijne in the publication "Identification of prokaryotic and eukaryotic signal peptides and prediction of their cleavage sites" Protein Engineering, Vol. 10, no. 1, pp. 1-6 (1997), incorporated herein by reference. A maximum S score and a mean S score, as described in the Nielson et al, as reference, were obtained for the polypeptide sequences. Table 6 shows the position of the last

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amino acid of the signal peptide in each of the polypeptides and the maximum score and mean score associated with that signal peptide.

Table 7 correlates each of SEQ ID NO: 1-93 to a specific chromosomal location.

Table 8 is a correlation table of the novel polynucleotide sequences SEQ ID NO: 1
93, novel polypeptide sequences SEQ ID NO: 94-186, and their corresponding priority nucleotide sequences in the priority application USSN 09/728,952, herein incorporated by reference in its entirety.

Library

SEQ ID NO:

TABLE 1

Tissue Origin

RNA/Tissue

1 133 uc Ot igin	ICAM IIIsauc	Libiary	DEQ ID NO.
	Source	Name	
adult brain	GIBCO	AB3001	26 40 43
adult brain	GIBCO	ABD003	2-5 40 47 54-55 57
adult brain	Clontech	ABR001	2 39 85
adult brain	Clontech	ABR006	3-4 40 47 69 80
adult brain	Clontech	ABR008	1 3-6 10 12 15-16 30-31 40 42 47 50 54-55
			57 67-68 72-74 86
adult brain	Invitrogen	ABR013	1
adult brain	Invitrogen	ABR015	47
brain	Invitrogen	ABR016	57
adult brain	Invitrogen	ABT004	10 15 42 47
cultured	Stratagene	ADP001	43
preadipocytes			
adrenal gland	Clontech	ADR002	2 24 39-40 43 46 50 56 68 73
adult heart	GIBCO	AHR001	2-5 14 40 43 49 60 64-65 71
adult kidney	GIBCO	AKD001	2 7 15 19 40 43-44 49-51 53 71 77
adult kidney	Invitrogen	AKT002	2-5 39-40 43 49-50 53 57 83 85
adult lung	GIBCO	ALG001	39-40 43-44 85
lymph node	Clontech	ALN001	38 44
young liver	GIBCO	ALV001	7
adult liver	Invitrogen	ALV002	7 9 38 43 47 52 82
adult liver	Clontech	ALV003	56
adult ovary	Invitrogen	AOV001	2-5 7 15-18 38-40 43-44 49 52 56-57 77 85
placenta	Invitrogen	APL002	44
adult spleen	GIBCO	ASP001	10 38 43 50 61-62
testis	GIBCO	ATS001	24 44 53 56
adult bladder	Invitrogen	BLD001	15 56
bone marrow	Clontech	BMD001	40-41 48 50 57-58
bone marrow	Clontech	BMD002	2-5 17-18 24 30-31 38 41 43 48 53-55 58-
			60 68 73 86
Mixture of 16	Various	CTL016	24
tissues- mRNAs	Vendors*		
adult cervix	BioChain	CVX001	11 15 39-40 54-55 63 66 71 77 82 85
endothelial cells	Stratagene	EDT001	2-4 15-16 40 43-44 47 50 57
fetal brain	Clontech	FBR006	2-6 10 13 16 31 42 46 49 66-68 73 78 86
fetal brain	Invitrogen	FBT002	24 44 47 61-62
fetal heart	Invitrogen	FHR001	43 68 73 77 86
fetal kidney	Clontech	FKD001	44 72
fetal kidney	Clontech	FKD002	49 66 77 88

Tissue Origin	RNA/Tissue	Library	SEQ ID NO:
	Source	Name	
fetal lung	Clontech	FLG001	64-65
fetal lung	Invitrogen	FLG003	15 39 63-65 71-72 85
fetal liver-spleen	Columbia	FLS001	2-5 7 9 22-24 26 35 38-41 44-46 49 51-52
	University		54-55 59-62 68 73 77 85 87
fetal liver-spleen	Columbia	FLS002	7 22-24 35 39-41 43-46 54-55 59-62 67 73
L	University		76 83-85
fetal liver-spleen	Columbia	FLS003	26
	University	· · · · · · · · · · · · · · · · · · ·	
fetal liver	Invitrogen	FLV001	22-24 44 49-50 52 61-62
fetal liver	Clontech	FLV004	41 68 73
fetal muscle	Invitrogen	FMS001	3-5 15 24 50 52
fetal muscle	Invitrogen	FMS002	56
fetal skin	Invitrogen	FSK001	3-5 15 22-24 39-40 44 51-53 57 61-62 79-
			82 85
fetal skin	Invitrogen	FSK002	3-5 31 49 72
fetal spleen	BioChain	FSP001	43
umbilical cord	BioChain	FUC001	3-5 10 15 39-40 44 72
fetal brain	GIBCO	HFB001	2 10 40 47 50 63 77 86
macrophage	Invitrogen	HMP001	43
infant brain	Columbia	IB2002	1 6 12 31 40 42 44 47 52 56 61-62 66 72 82
	University		86
infant brain	Columbia	IB2003	50 56 86
	University		
infant brain	Columbia	IBS001	72
	University		
fibroblast	Stratagene	LFB001	39-40 49 57
lung tumor	Invitrogen	LGT002	3-5 38-40 43 49 54-57 85
lymphocytes	ATCC	LPC001	58
leukocyte	GIBCO	LUC001	3-5 15 17-19 26 31 38 43-44 50 54-55 58
leukocyte	Clontech	LUC003	41 43
melanoma from cell	Clontech	MEL004	2 57
line ATCC #CRL			
1424	Ŧ	10.60001	2.5.15.22.23.24.25.22.24.25.25.24.25.25.25.25.25.25.25.25.25.25.25.25.25.
mammary gland	Invitrogen	MMG001	3-5 15 30 38 43-44 47 50 54-57 71
induced neuron cells	Stratagene	NTD001	42
neuronal cells		NITT IOO 1	1.04.40.50
	Stratagene	NTU001	1 24 42 72
pituitary gland	Clontech	PIT004	47
placenta	Clontech	PLA003	14 19 43 63-65
rectum salivary gland	Invitrogen	REC001	10 22-24 61-62 68 73
small intestine	Clontech	SAL001	40
	Clontech	SIN001	2 22-24 30 66 68-69 73 84
skeletal muscle	Clontech	SKM001	3-5 40 51
spinal cord	Clontech	SPC001	40 45 50 70
adult spleen	Clontech	SPLc01	8 15-16 40 43 68 73 86
stomach	Clontech	STO001	57-58 75
thalamus	Clontech	THA 002	30 51 57 82
thymus	Clontech	THM001	2-5 24 43 86
thymus	Clontech	THMc02	2 15 33 38 44 46 48-49 66 73 86
thyroid gland	Clontech	THR001	2 7 15 39-40 54-55 58 69 71 86-87
trachea	Clontech	TRC001	44 54-55
uterus	Clontech	UTR001	8

The 16 tissue/mRNAs and their vendor sources are as follows: 1) Normal adult brain mRNA (Invitrogen), 2) Normal adult kidney mRNA (Invitrogen), 3) Normal fetal brain mRNA (Invitrogen), 4) Normal adult liver mRNA (Invitrogen), 5) Normal fetal kidney mRNA (Invitrogen), 6) Normal fetal liver mRNA (Invitrogen), 7) normal fetal skin mRNA (Invitrogen), 8) human adrenal gland mRNA (Clontech), 9) Human bone marrow mRNA (Clontech), 10) Human leukemia lymphoblastic mRNA (Clontech), 11) Human thymus mRNA (Clontech), 12) human lymph node mRNA (Clontech), 13) human so\spinal cord mRNA (Clontech), 14) human thyroid mRNA (Clontech), 15) human esophagus mRNA (BioChain), 16) human conceptional umbilical cord mRNA (BioChain).

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TABLE 2

SEQ ID NO:	Accession No.	Species	Description	Score	% Identity
94	gi15080005	Homo sapiens	nogo receptor, clone MGC:19831 IMAGE:4040540, mRNA, complete cds.	1305	100
94	gi12407653	Homo sapiens	Nogo receptor mRNA, complete cds.	1305	100
94	gi15385806	Homo sapiens	Predicted human Nogo receptor gene	1305	100
95	AAB53348	Homo sapiens	Human colon cancer antigen protein sequence SEQ ID NO:888.	1864	99
95	AAG73782	Homo sapiens	Human colon cancer antigen protein SEQ ID NO:4546.	1864	99
95	gi15928738	Mus musculus	RIKEN cDNA 1110064N10 gene	1407	94
96	gi5531827	Homo sapiens	p47	1694	98
96	gi12803909	Homo sapiens	p47, clone MGC:3347 IMAGE:3635947, mRNA, complete cds.	1689	98
96	gi8979825	Homo sapiens	Human DNA sequence from clone RP4-776F14 on chromosome 20p12.2-13. Contains the 5' end of the FKBP1A gene for FK506-binding protein 1A (12kD), the gene for P47 protein, part of a novel member of the PTPNS (protein tyrosine phosphatase, non-receptor type substrate 1) gene family, ESTs, STSs, GSSs and two CpG islands, complete sequence.	1689	98
97	gi7022811	Homo sapiens	cDNA FLJ10649 fis, clone NT2RP2005835, weakly similar to SHP1 PROTEIN.	1541	99
97	AAB93031	Homo sapiens	Human protein sequence SEQ ID NO:11803.	1541	99

SEQ ID NO:	Accession No.	Species	Description	Score	% Identity
97	gi6563210	Homo sapiens	p47 protein mRNA, complete cds.	813	90
98	AAB42552	Homo sapiens	Human ORFX ORF2316 polypeptide sequence SEQ ID NO:4632.	826	90
98	AAB12868	Homo sapiens	Human P47 amino acid sequence.	815	89
98	gi12803909	Homo sapiens	p47, clone MGC:3347 IMAGE:3635947, mRNA, complete cds.	806	89
99	gi12836289	Mus musculus	putative	347	68
99	gi1006665	Homo sapiens	H.sapiens mRNA for transcript associated with monocyte to macrophage differentiation.	346	68
99	gi7290797	Drosophila melanogaster	CG4615 gene product	159	37
100	gi7020785	Homo sapiens	cDNA FLJ20581 fis, clone REC00491.	2996	99
100	gi2988399	Homo sapiens	Chromosome 16 BAC clone CIT987SK-44M2, complete sequence.	1874	60
100	gi666014	Homo sapiens	Human SA mRNA for SA gene product, complete cds.	1873	60
101	gi5915662	Homo sapiens	integrin alpha 11 subunit precursor (ITGA11) mRNA, complete cds.	497	98
101	AAB30929	Homo sapiens	Amino acid sequence of a human alpha11 integrin chain.	497	98
101	AAB50085	Homo sapiens	Human A259.	497	98
102	gi431608	Oncorhynchus mykiss	complement component C3	223	30
102	gi213373	Naja naja	complement component C3	209	29
102	gi755815	Gallus gallus	complement C3 precursor	206	31
103	gi7020791	Homo sapiens	cDNA FLJ20584 fis, clone KAT09532.	1052	100
103	gi14250646	Homo sapiens	Similar to hypothetical protein FLJ20584, clone MGC:3446 IMAGE:3627081, mRNA, complete cds.	810	89
103	gi13278391	Mus musculus	Similar to hypothetical protein FLJ20584	729	70
104	gi10799397	Homo sapiens	chromosome 19, BAC BC349142 (CTC-518B2), complete sequence.	1404	99
104	gi6249632	Homo sapiens	kallikrein-like protein 5 gene, alternative splice products, complete cds.	1404	99
104	gi11244770	Homo sapiens	serine protease gene cluster, complete sequence.	1301	100
105	gi12310959	Homo sapiens	unnamed protein product	2095	100
105	AAY33741	Homo sapiens	Beta-secretase.	1694	99
105	AAB61142	Homo sapiens	Human NOV12 protein.	2088	99
106	gi14017771	Homo sapiens	mRNA for KIAA1776 protein (fibrillin3), complete cds.	2940	55
106	gi762831	Mus musculus	fibrillin 2	2153	50
106	gi3688648	Mus musculus	mutant fibrillin-1	2102	46

SEQ ID NO:	Accession No.	Species	Description	Score	% Identity
107	AAB24199	Homo sapiens	Human GTP-binding protein- coupled receptor BG3 protein sequence.	925	100
107	gi7328047	Homo sapiens	mRNA; cDNA DKFZp434B1272 (from clone DKFZp434B1272); partial cds.	760	100
107	AAB01249	Homo sapiens	Human EMR1 hormone receptor.	254	41
108	AAY93948	Homo sapiens	Amino acid sequence of a lectin ss3939 polypeptide.	1979	98
108	AAE03651	Homo sapiens	Human extracellular matrix and cell adhesion molecule-15 (XMAD-15).	1979	98
108	AAY91490	Homo sapiens	Human secreted protein sequence encoded by gene 40 SEQ ID NO:163.	1969	98
109	gi6979311	Homo sapiens	cysteine-rich repeat-containing protein S52 precursor, mRNA, complete cds.	2875	99
109	AAY82776	Homo sapiens	Human chordin related protein (Clone dj167_19).	2875	99
109	AAY53034	Homo sapiens	Human secreted protein clone dj167_19 protein sequence SEQ ID NO:74.	2875	99
110	AAW99070	Homo sapiens	Human PIGR-1.	678	100
110	gi12405479	Homo sapiens	unnamed protein product	672	99
110	AAB31568	Homo sapiens	Amino acid sequence of human leukocyte surface receptor (LSR).	672	99
111	AAW99070	Homo sapiens	Human PIGR-1.	612	100
111	gi12405479	Homo sapiens	unnamed protein product	606	99
111	AAB31568	Homo sapiens	Amino acid sequence of human leukocyte surface receptor (LSR).	606	99
112	gi9663958	Homo sapiens	mRNA for cysteinyl leukotriene CysLT2 receptor, complete cds; cDNA: PSEC0146 from clone PLACE1006979.	1788	100
112	gi10442008	Homo sapiens	cysteinyl leukotriene receptor CYSLT2 gene, complete cds.	1788	100
112	gi14582394	Homo sapiens	cysteinyl leukotriene receptor type 2 (CYSLT2) gene, complete cds.	1788	100
113	gi4580013	Homo sapiens	TRAF4-associated factor 2 mRNA, partial cds.	1432	70
113	gi4689252	Homo sapiens	sorting nexin 6 (SNX6) mRNA, complete cds.	1432	70
113	AAB58368	Homo sapiens	Lung cancer associated polypeptide sequence SEQ ID 706.	1432	70
114	gi14042571	Homo sapiens	cDNA FLJ14791 fis, clone NT2RP4001064, weakly similar to SYNAPTONEMAL COMPLEX PROTEIN SC65.	3090	92
114	gi14272600	Homo sapiens	unnamed protein product	3090	92
114	AAB93215	Homo sapiens	Human protein sequence SEQ	3090	92

SEQ ID NO:	Accession No.	Species	Description	Score	% Id-adia
NO:			ID NO:12194.	-	Identity
115	gi12053261	Homo sapiens	mRNA; cDNA DKFZp434A196 (from clone DKFZp434A196); complete cds.	1502	76
115	gi9754902	Mus musculus	espin	1462	78
115	gi5327035	Homo sapiens	Human DNA sequence from clone 20208 on chromosome 1p36.11-36.31. Contains the 5' part of a gene for a novel rat Espin LIKE protein containing Ank repeats, the gene for the ortholog of rodent HES2 (Hairy and Enhacer of Split 2) and the 5' end of the gene for HBACH (Brain Acyl-CoA Hydrolase (Acyl Coenzyme A Thioester Hydrolase, EC 3.1.2.2). Contains ESTs, GSSs and putative CpG islands, complete sequence.	2451	69
116	gi5327035	Homo sapiens	Human DNA sequence from clone 202O8 on chromosome 1p36.11-36.31. Contains the 5' part of a gene for a novel rat Espin LIKE protein containing Ank repeats, the gene for the ortholog of rodent HES2 (Hairy and Enhacer of Split 2) and the 5' end of the gene for HBACH (Brain Acyl-CoA Hydrolase (Acyl Coenzyme A Thioester Hydrolase, EC 3.1.2.2). Contains ESTs, GSSs and putative CpG islands, complete sequence.	3530	91
116	gi4375916	Homo sapiens	H.sapiens gene from PAC 163M9, similar to rat Espin gene, partial cds.	3333	93
116	gi3320122	Rattus norvegicus	espin	3269	75
117	AAE01020	Homo sapiens	Human pif-1 type helicase protein.	1875	78
117	gi5523990	Homo sapiens	DNA helicase homolog (PIF1) mRNA, partial cds.	1842	97
117	gi7295800	Drosophila melanogaster	CG3238 gene product	1196	46
118	AAE01020	Homo sapiens	Human pif-1 type helicase protein.	911	99
118	gi5523990	Homo sapiens	DNA helicase homolog (PIF1) mRNA, partial cds.	834	85
118	gi7295800	Drosophila melanogaster	CG3238 gene product	620	46
119	gi10434929	Homo sapiens	cDNA FLJ13080 fis, clone NT2RP3002007, weakly similar to SAP1 PROTEIN.	3490	99
119	AAB94461	Homo sapiens	Human protein sequence SEQ ID NO:15114.	3490	99
119	AAB95164	Homo sapiens	Human protein sequence SEQ	3483	99

SEQ ID NO:	Accession No.	Species	Description	Score	% Identity
			ID NO:17211.		
120	gi29715	Homo sapiens	Human mRNA for pro-cathepsin L (major excreted protein MEP).	1597	87
120	gi190418	Homo sapiens	Human cathepsin L gene, complete cds.	1597	87
120	AAW47031	Homo sapiens	Human procathepsin L.	1597	87
121	AAG63220	Homo sapiens	Amino acid sequence of a human lipid metabolism enzyme.	4116	99
121	gi15862521	Homo sapiens	unnamed protein product	3834	99
121	gi14715017	Homo sapiens	Similar to phospholipase C, delta, clone MGC:9744 IMAGE:3854215, mRNA, complete cds.	3195	99
122	gi13676465	Macaca fascicularis	hypothetical protein	495	41
122	gi2253280	Bos taurus	butyrophilin	490	44
122	gi162773	Bos taurus	butyrophilin precursor	487	44
123	AAB25682	Homo sapiens	Human secreted protein sequence encoded by gene 18 SEQ ID NO:71.	1616	96
123	gi2982501	Homo sapiens	mRNA for neuropathy target esterase.	952	65
123	AAY70474	Homo sapiens	Human cyclic nucleotide- associated protein-2 (CNAP-2).	952	65
124	AAB24084	Homo sapiens	Human PRO1317 protein sequence SEQ ID NO:71.	1739	100
124	AAB37984	Homo sapiens	Human secreted protein encoded by gene 1 clone HTDAA93.	1739	100
124	AAY99418	Homo sapiens	Human PRO1317 (UNQ783) amino acid sequence SEQ ID NO:277.	1739	100
126	gi292057	Homo sapiens	Human EBV induced G-protein coupled receptor (EBI2) mRNA, complete cds.	196	40
126	AAR54080	Homo sapiens	Epstein Barr virus induced (EBI-2) polypeptide.	196	40
126	AAW53623	Homo sapiens	Epstein Barr virus induced gene 2 (EBI-2).	196	40
127	gi63426	Gallus gallus	lysozyme	428	43
127	gi12843551	Mus musculus	putative	367	41
127	gi12578467	Homo sapiens	unnamed protein product	366	40
128	gi 13 195239	Homo sapiens	complement factor H-related protein 5 mRNA, complete cds.	1492	100
128	gi180498	Homo sapiens	Human complement H factor mRNA, complete cds.	585	51
128	gi309166	Mus musculus	complement factor H-related protein	583	44
129	gi11275568	Homo sapiens	mucin 5B (MUC5B) gene, partial cds.	7389	99
129	gi3789927	Homo sapiens	mucin (MUC5B) mRNA, partial cds.	7176	97
129	gi4038587	Homo sapiens	partial MUC5B gene, exon 1-29.	7151	98
130	gi2853301	Homo sapiens	mucin (MUC3) mRNA, partial cds.	3473	77
130	gi6466801	Homo sapiens	intestinal mucin 3 (MUC3) gene,	3218	76

SEQ ID NO:	Accession No.	Species	Description	Score	% Identity
			partial cds.		
130	gi9929920	Homo sapiens	MUC3A mRNA for intestinal mucin, partial cds.	2904	100
131	gi1235725	Homo sapiens	mRNA for macrophage lectin 2, complete cds.	1014	79
131	gi204303	Rattus norvegicus	Gal/GalNAc-specific lectin precursor	879	55
131	gi15928688	Mus musculus	Similar to macrophage galactose N-acetyl-galactosamine specific lectin	806	51
132	AAB43122	Homo sapiens	Human ORFX ORF2886 polypeptide sequence SEQ ID NO:5772.	3123	94
132	gi11177164	Mus musculus	polydom protein	2668	77
132	gi14198157	Mus musculus	polydomain protein	2668	77
133	gi7110160	Homo sapiens	guanine nucleotide exchange factor (LARG) mRNA, complete cds.	7932	99
133	AAW64468	Homo sapiens	Human secreted protein from clone CW420_2.	6937	99
133	AAB90743	Homo sapiens	Human CW420_2 protein sequence SEQ ID 186.	6937	99
134	AAM00758	Homo sapiens	Human bone marrow protein, SEQ ID NO: 121.	1804	100
134	gi13937956	Homo sapiens	clone MGC:14710 IMAGE:4250452, mRNA, complete cds.	1677	67
134	gi32645	Homo sapiens	Human mRNA for 56-KDa protein induced by interferon.	1671	67
135	gi4580013	Homo sapiens	TRAF4-associated factor 2 mRNA, partial cds.	1432	70
135	gi4689252	Homo sapiens	sorting nexin 6 (SNX6) mRNA, complete cds.	1432	70
135	AAB58368	Homo sapiens	Lung cancer associated polypeptide sequence SEQ ID 706.	1432	70
136	gi6165618	Homo sapiens	gamma-interferon inducible lysosomal thiol reductase (GILT) mRNA, complete cds.	1149	100
136	AAB58455	Homo sapiens	Lung cancer associated polypeptide sequence SEQ ID 793.	1149	100
136	AAY71214	Homo sapiens	Human irritable bowel disease related polypeptide IMX44.	1142	99
137	gi14042571	Homo sapiens	cDNA FLJ14791 fis, clone NT2RP4001064, weakly similar to SYNAPTONEMAL COMPLEX PROTEIN SC65.	3090	92
137	gi14272600	Homo sapiens	unnamed protein product	3090	92
137	AAB93215	Homo sapiens	Human protein sequence SEQ ID NO:12194.	3090	92
138	gi35330	Homo sapiens	H.sapiens mRNA for procarboxypeptidase A1.	1198	97
138	gi2299431	unidentified	unnamed protein product	1198	97
138	AAW01504	Homo sapiens	Wild-type human pancreatic carboxypeptidase 1.	1198	97

SEQ ID	Accession No.	Species	Description	Score	%
NO: 139	gi12053081	Homo sapiens	mRNA; cDNA DKFZp434L0718 (from clone DKFZp434L0718); complete cds.	2766	Identity 100
139	AAY10853	Homo sapiens	Amino acid sequence of a human secreted protein.	417	87
139	AAB42173	Homo sapiens	Human ORFX ORF1937 polypeptide sequence SEQ ID NO:3874.	202	39
141	AAB93455	Homo sapiens	Human protein sequence SEQ ID NO:12712.	546	100
141	gi599683	Bos taurus	Cleavage and Polyadenylation specificity factor (CPSF) 100kD subunit	546	100
141	gi2331036	Mus musculus	cleavage and polyadenylation specificity factor	538	98
142	gi29715	Homo sapiens	Human mRNA for pro-cathepsin L (major excreted protein MEP).	1597	87
142	gi190418	Homo sapiens	Human cathepsin L gene, complete cds.	1597	87
142	AAW47031	Homo sapiens	Human procathepsin L.	1597	87
143	gi1103582	Homo sapiens	H.sapiens mRNA for ARP1 protein.	1055	100
143	gi9843764 gi7012932	Homo sapiens	Human DNA sequence from clone RP4-583P15 on chromosome 20 Contains ESTs, STSs, GSSs and ten CpG islands. Contains the TNFRSF6B gene for tumor necrosis factor receptor 6b (decoy), the 3' part of the KIAA1088 gene, the ARFRP1 gene for ADP-ribosylation factor related protein 1, two genes for novel proteins, the gene for a GLUT4 enhancer factor and the gene for a novel zinc finger protein similar to rat RIN ZF and the gene for a novel BTB/POZ domain containing zinc finger protein, complete sequence. SCG10 like-protein, helicase-	1055	100
		-	like protein NHL, M68, and ADP-ribosylation factor related protein 1 (ARFRP1) genes, complete cds.		
144	gi13623501	Homo sapiens	clone MGC:12837 IMAGE:4124286, mRNA, complete cds.	1008	100
144 .	gi571466	Rattus norvegicus	phospholipase C delta-4	741	73
144	gi1304189	Rattus norvegicus	phodpholipase C delta4	734	72
145	gi12053129	Homo sapiens	mRNA; cDNA DKFZp434C2322 (from clone DKFZp434C2322); complete	1185	100

SEQ ID NO:	Accession No.	Species	Description	Score	% Identity
			cds.	l	
145	gi16117338	Homo sapiens	vWF-CP(ADAMTS13) mRNA for von Willebrand factor- cleaving protease, complete cds.	1185	100
145	gi15963593	Homo sapiens	ADAMTS13 (ADAMTS13) mRNA, complete cds, alternatively spliced.	1185	100
146	gi6624133	Homo sapiens	PAC clone RP4-539M6 from 22, complete sequence.	322	98
146	gi4164418	Rattus norvegicus	45 kDa secretory protein	247	75
146	gi13543184	Mus musculus	Unknown (protein for MGC:6302)	245	75
147	AAB98640	Homo sapiens	Human autoimmune disease associated protein 16.	766	99
147	gi7768747	Homo sapiens	genomic DNA, chromosome 21q, section 92/105.	292	68
147	gi12654677	Homo sapiens	U2(RNU2) small nuclear RNA auxillary factor 1 (non-standard symbol), clone MGC:2223 IMAGE:3534272, mRNA, complete cds.	292	68
148	AAB98640	Homo sapiens	Human autoimmune disease associated protein 16.	757	98
148	gi7768747	Homo sapiens	genomic DNA, chromosome 21q, section 92/105.	691	79
148	gi12654677	Homo sapiens	U2(RNU2) small nuclear RNA auxillary factor 1 (non-standard symbol), clone MGC:2223 IMAGE:3534272, mRNA, complete cds.	691	79
149	AAG63220	Homo sapiens	Amino acid sequence of a human lipid metabolism enzyme.	4116	99
149	gi15862521	Homo sapiens	unnamed protein product	3834	99
149	gi14715017	Homo sapiens	Similar to phospholipase C, delta, clone MGC:9744 IMAGE:3854215, mRNA, complete cds.	3195	99
150	gi11493982	Homo sapiens	TLH29 protein precursor (TLH29) mRNA, complete cds.	538	95
150	AAY12410	Homo sapiens	Human 5' EST secreted protein SEQ ID NO:441.	527	94
150	AAG89188	Homo sapiens	Human secreted protein, SEQ ID NO: 308.	505	98
151	gil1863671	Homo sapiens	mRNA for putative tumor stroma and activated macrophage protein DLM-1 (DLM-1 gene).	1362	99
151	gi13160377	Homo sapiens	Human DNA sequence from clone RP4-718J7 on chromosome 20q13.31-13.33 Contains the PCK1 gene for soluble phosphoenolpyruvate carboxykinase 1, part of a novel gene similar to mouse DLM-1	1246	94

SEQ ID NO:	Accession No.	Species	Description	Score	% Identity
			(tumour stroma and activated macrophage protein), the 3' end of the TMEPAI gene encoding an androgen induced 1b transmembrane protein (PMEPAI), two putative novel genes, a CpG island, ESTs, STSs and GSSs, complete sequence.		
151	gi6563280	Mus musculus	tumor stroma and activated macrophage protein DLM-1	565	51
152	gi13592175	Leishmania major	ppg3	220	26
152	gi601930	Oryctolagus cuniculus	neurofilament-H	184	25
152	gi5420387	Leishmania major	proteophosphoglycan	186	26 .
153	AAB42658	Homo sapiens	Human ORFX ORF2422 polypeptide sequence SEQ ID NO:4844.	8542	99
153	gi15077826	Homo sapiens	rap guanine nucleotide exchange factor mRNA, complete cds.	7521	98
153	gi6650766	Homo sapiens	PDZ domain-containing guanine nucleotide exchange factor I mRNA, complete cds.	6208	100
154	gi1657312	Homo sapiens	H.sapiens mRNA for FAA protein.	7165	98
154	AAW48663	Homo sapiens	Fanconi anaemia of complementation group A protein.	7165	98
154	gi2230888	Homo sapiens	H.sapiens Fanconi anaemia group A gene, exon 1 and joined CDS.	7162	98
155	gi1657312	Homo sapiens	H.sapiens mRNA for FAA protein.	4876	100
155	AAW48663	Homo sapiens	Fanconi anaemia of complementation group A protein.	4876	100
155	gi2230888	Homo sapiens	H.sapiens Fanconi anaemia group A gene, exon 1 and joined CDS.	4873	99
156	AAB60469	Homo sapiens	Human cell cycle and proliferation protein CCYPR-17, SEQ ID NO:17.	846	100
156	AAY76403	Homo sapiens	Fragment of human secreted protein encoded by gene 85.	600	100
156	gi12861086	Mus musculus	putative	512	66
157	gi16041826	Homo sapiens	interferon regulatory factor 2, clone MGC:9260 IMAGE:3920890, mRNA, complete cds.	1626	100
157	gi33967	Homo sapiens	Human mRNA for interferon regulatory factor-2 (IRF-2).	1612	99
157	AAB70698	Homo sapiens	Human IRF-2 protein sequence `SEQ ID NO:7.	1612	99
158	gi16041826	Homo sapiens	interferon regulatory factor 2, clone MGC:9260	892	100

SEQ ID NO:	Accession No.	Species	Description	Score	% Identity
			IMAGE:3920890, mRNA, complete cds.		
158	gi33967	Homo sapiens	Human mRNA for interferon regulatory factor-2 (IRF-2).	892	100
158	AAB70698	Homo sapiens	Human IRF-2 protein sequence SEQ ID NO:7.	892	100
159	gi7637906	Homo sapiens	Ral guanine nucleotide exchange factor RalGPS1A mRNA, complete cds.	2768	100
159	gi2224643	Homo sapiens	Human mRNA for KIAA0351 gene, complete cds.	1758	100
159	gi11321424	Mus musculus	Ral-A exchange factor RalGPS2	1228	70
160	gi7716046	Mus musculus	regulator factor X 5	606	38
160	gi840789	Homo sapiens	H.sapiens mRNA for DNA binding regulatory factor.	580	35
160	AAB40374	Homo sapiens	Human ORFX ORF138 polypeptide sequence SEQ ID NO:276.	565	98
161	gi13436464	Homo sapiens	Similar to cleavage and polyadenylation specific factor 6, 68kD subunit, clone MGC:4425 IMAGE:2958189, mRNA, complete cds.	364	48
161	gi12653847	Homo sapiens	Similar to cleavage and polyadenylation specific factor 6, 68kD subunit, clone MGC:1242 IMAGE:3506481, mRNA, complete cds.	364	48
161	gi871299	Homo sapiens	H.sapiens HPBRII-4 mRNA.	359	47
162	gi4699969	Homo sapiens	PAC clone RP4-568B10 from 7q31.1-q31.2, complete sequence.	1379	99
162	gi13876344	Mus musculus	protocadherin gamma A9	265	28
162	gi14625441	Homo sapiens	mRNA for KIAA1773 protein (dachsous homologue), complete cds.	246	29
163	gi7959299	Homo sapiens	mRNA for KIAA1516 protein, partial cds.	8192	99
163	gi11065786	Homo sapiens	phospholipase C epsilon mRNA, partial cds.	8186	99
163	gi10518469	Homo sapiens	phosphoinositide-specific phospholipase C PLC-epsilon mRNA, complete cds.	8127	99
164	gi386827	Homo sapiens	Human inhibin beta-B-subunit gene, exon 2, and complete cds.	2197	99
164	AAY92017	Homo sapiens	Human inhibin B beta subunit.	2197	99
164	AAY92019	Homo sapiens	Human activin B subunit.	2197	99
165	gi16040975	Homo sapiens	HIF-3A mRNA for hypoxia- inducible factor-3 alpha, complete cds.	1480	99
165	gi4558637	Homo sapiens	chromosome 19, BAC 82621 (CIT-B-139a18), complete sequence.	1480	99
165	gi14042618	Homo sapiens	cDNA FLJ14819 fis, clone OVARC1000241, moderately similar to HYPOXIA-	1476	98

SEQ ID NO:	Accession No.	Species	Description	Score	% Identity
			INDUCIBLE FACTOR 1 ALPHA.		
166	gi10434070	Homo sapiens	cDNA FLJ12529 fis, clone NT2RM4000156, weakly similar to H.sapiens HPBRII-7 gene.	975	98
166	AAB94099	Homo sapiens	Human protein sequence SEQ ID NO:14318.	975	98
166	gi13436464	Homo sapiens	Similar to cleavage and polyadenylation specific factor 6, 68kD subunit, clone MGC:4425 IMAGE:2958189, mRNA, complete cds.	883	48
167	gi7533125	Homo sapiens	fibroblast growth factor receptor 3 (FGFR3) mRNA, complete cds, alternatively spliced.	3664	100
167	gi211443	Gallus gallus	cek2 protein	1842	92
167	gi186782	Homo sapiens	Human secreted fibroblast growth factor receptor (K-sam- III) mRNA, complete cds.	2482	73
169	gi13543469	Homo sapiens	Similar to Natriuretic peptide precursor A, (pronatriodilatin, also Anf, Pnd), clone MGC:14467 IMAGE:4273949, mRNA, complete cds.	181	97
169	gi3171893	Homo sapiens	DNA sequence from PAC 934G17 on chromosome 1p36.21. Contains the alternatively spliced CLCN6 gene for chloride chanel proteins CLC-6A (KIAA0046) -B, -C and -D, the alternatively spliced NPPA gene coding for Atrial Natriuretic Factor ANF precursor (Atrial Natriuretic peptide ANP, Prepronatriodilatin), the NPPB gene for Brain Natriuretic Protein BNP, and a pseudogene similar to SBF1 (and other Myotubularin-related protein genes). Contains ESTs, STSs and the genomic marker D1S2740, complete sequence.	181	97
169	gi825625	Homo sapiens	Human gene fragment for pronatriodilatin precursor (exons 1 and 2).	181	97
170	gi13274524	Homo sapiens	complement-clq tumor necrosis factor-related protein (CTRP7) mRNA, complete cds.	1576	100
170	gi12228258	Homo sapiens	unnamed protein product	1576	100
170	AAB50371	Homo sapiens	Human ZACRP7.	1576	100
171	AAB08783	Homo sapiens	Amino acid sequence of a human serpin polypeptide.	742	87
171	gi2077914	Bos taurus	thrombin inhibitor	516	67
171	gi12655087	Homo sapiens	serine (or cysteine) proteinase inhibitor, clade B (ovalbumin),	511	66

SEQ ID NO:	Accession No.	Species	Description	Score	% Identity
			member 6, clone MGC:2180 IMAGE:3051381, mRNA, complete cds.		
172	gi63426	Gallus gallus	lysozyme	428	43
172	gi12843551	Mus musculus	putative	367	41
172	gi12578467	Homo sapiens	unnamed protein product	366	40
173	gi2443367	Homo sapiens	mRNA for Nck, Ash and phospholipase C gamma-binding protein NAP4, partial cds.	2432	100
173	A A W02275	Home conions	Human SOCS19 protein.	2432	100
173	AAW93275 AAW62623	Homo sapiens Homo sapiens	Homo sapiens SOCS11 protein.	953	100
174		Mus musculus		414	97
174	gi12834584 gi7582391	Mus musculus	putative p53 apoptosis-associated target	414	97
174	AAB70474	Homo sapiens	PERP (p53 apoptosis effector related to PMP-22) protein sequence.	414	97
175	gi12834584	Mus musculus	putative	1054	99
175	gi7582391	Mus musculus	p53 apoptosis-associated target	1054	99
175	AAY33261	Homo sapiens	Human p99 protein.	1054	99
176	AAB95035	Homo sapiens	Human protein sequence SEQ ID NO:16788.	221	62
177	gi6650766	Homo sapiens	PDZ domain-containing guanine nucleotide exchange factor I mRNA, complete cds.	243	87
177	gi15077826	Homo sapiens	rap guanine nucleotide exchange factor mRNA, complete cds.	243	87
177	AAB42658	Homo sapiens	Human ORFX ORF2422 polypeptide sequence SEQ ID NO:4844.	243	87
178	AAB43122	Homo sapiens	Human ORFX ORF2886 polypeptide sequence SEQ ID NO:5772.	3099	94
178	gi11177164	Mus musculus	polydom protein	3095	79
178	gi14198157	Mus musculus	polydomain protein	3095	79
179	gi6572379	Homo sapiens	Human DNA sequence from clone 579N16 on chromosome 22. Contains the 3' part of the gene for KIAA0685, the SBF1 gene for SET binding factor 1, a novel gene, ESTs, an STS, GSSs and three putative CpG islands, complete sequence.	8482	99
179	gi3015538	Homo sapiens	nuclear dual-specificity phosphatase (SBF1) mRNA, partial cds.	8315	98
179	gi12698077	Homo sapiens	mRNA for KIAA1766 protein, partial cds.	3621	62
180	gi1234787	Xenopus laevis	up-regulated by thyroid hormone in tadpoles; expressed specifically in the tail and only at metamorphosis; membrane bound or extracellular protein; C-terminal basic region	1563	69
180	gi10435980	Homo sapiens	cDNA FLJ13840 fis, clone THYRO1000783, moderately similar to Xenopus laevis tail-	1562	94

SEQ ID NO:	Accession No.	Species	Description	Score	% Identity
			specific thyroid hormone up- regulated (gene 5) mRNA.		
180	AAB94773	Homo sapiens	Human protein sequence SEQ ID NO:15860.	1562	94
181	gi12848947	Mus musculus	putative	582	60
181	gi5453324	Mus musculus	syntaxin4-interacting protein synip	576	59
181	AAB57636	Homo sapiens	Af-6 protein PDZ domain.	143	35
182	gi14041850	Homo sapiens	cDNA FLJ14369 fis, clone HEMBA1001174, highly similar to ADP-RIBOSYLATION FACTOR-LIKE PROTEIN 5.	940	100
182	gi12855057	Mus musculus	putative	940	100
182	AAB92480	Homo sapiens	Human protein sequence SEQ ID NO:10563.	940	100
183	gi11275568	Homo sapiens	mucin 5B (MUC5B) gene, partial cds.	7389	99
183	gi3789927	Homo sapiens	mucin (MUC5B) mRNA, partial cds.	7176	97
183	gi4038587	Homo sapiens	partial MUC5B gene, exon 1-29.	7151	98
184	gi2853301	Homo sapiens	mucin (MUC3) mRNA, partial cds.	3473	77
184	gi6466801	Homo sapiens	intestinal mucin 3 (MUC3) gene, partial cds.	3218	76
184	gi9929920	Homo sapiens	MUC3A mRNA for intestinal mucin, partial cds.	2904	100
185	gi6492116	Homo sapiens	carboxylesterase-related protein mRNA, complete cds.	210	61
185	gi550147	Rattus norvegicus	carboxylesterase ES-3 (egasyn)	215	62
185	gi15929734	Mus musculus	Similar to carboxylesterase 2 (intestine, liver)	207	59
186	gi854065	Human herpesvirus 6	U88	540	54
186	gi10434098	Homo sapiens	cDNA FLJ12547 fis, clone NT2RM4000634.	417	44
186	AAB95124	Homo sapiens	Human protein sequence SEQ ID NO:17122.	417	44 ,

TABLE 3

SEQ ID NO:	Accession No.	Description	Results*
102	BL00477	Alpha-2-macroglobulin family thiolester region proteins.	BL00477J 19.04 6.604e-19 15-46
104	BL00134	Serine proteases, trypsin family, histidine proteins.	BL00134B 15.99 5.154e-25 194-218 BL00134A 11.96 7.158e-19 47-64
104	BL00021	Kringle domain proteins.	BL00021B 13.33 1.000e-16 47-65
104		CHYMOTRYPSIN SERINE PROTEASE FAMILY (S1) SIGNATURE	PR00722A 12.27 3.348e-16 48-64 PR00722C 10.87 4.000e-16 193-206
104	PR00722	Type I fibronectin domain proteins.	BL01253G 11.34 9.234e-18 193-207 BL01253D 4.84 4.877e-11 47-61
104	BL00495	Apple domain proteins.	BL00495K 12.58 5.631e-09 49-82 BL00495N 11.04 6.919e-09 186-221
105	PD02327	GLYCOPROTEIN ANTIGEN PRECURSOR IMMUNOGLO.	PD02327B 19.84 4.098e-10 154-176
105	PR00442	G-PROTEIN ALPHA SUBUNIT GROUP Q SIGNATURE	PR00442E 7.23 1.740e-09 292-301
105	PR00440	G-PROTEIN ALPHA SUBUNIT GROUP 12 SIGNATURE	PR00440E 11.16 3.192e-09 292-301
105	DM00179	w KINASE ALPHA ADHESION T-CELL.	DM00179 13.97 6.478e-09 106-116 DM00179 13.97 9.609e-09 298-308
106	BL00243	Integrins beta chain cysteine-rich domain proteins.	BL00243H 17.53 4.391e-11 162-188
106	DM00864	EGF-LIKE DOMAIN.	DM00864B 11.34 5.836e-10 878-897
106	PR00907	THROMBOMODULI N SIGNATURE	PR00907G 11.63 5.366e-11 955-982 PR00907G 11.63 5.366e-11 1092-1119 PR00907G 11.63 9.066e-10 1356-1383 PR00907G 11.63 3.351e-09 1314-1341
106	PR00010	TYPE II EGF-LIKE SIGNATURE	PR00010C 11.16 3.250e-12 920-931 PR00010A 11.79 7.923e-11 490-502 PR00010C 11.16 5.071e-09 1404-1415 PR00010C 11.16 6.571e-09 1361-1372
106	BL00203	Vertebrate metallothioneins proteins.	BL00203 13.94 7.520e-09 1388-1434
106	BL01187	Calcium-binding EGF- like domain proteins pattern proteins.	BL01187B 12.04 1.000e-15 915-931 BL01187B 12.04 8.412e-15 1482-1498 BL01187B 12.04 7.750e-14 546-562 BL01187B 12.04 7.750e-14 1356-1372 BL01187A 9.98 4.214e-13 939-951 BL01187B 12.04 4.913e-13 873-889 BL01187B 12.04 4.913e-13 1399-1415 BL01187A 9.98 1.000e- 12 488-500 BL01187B 12.04 8.000e-12 465- 481 BL01187B 12.04 1.900e-11 1314-1330 BL01187B 12.04 3.100e-11 1441-1457 BL01187B 12.04 4.600e-11 504-520

SEQ ID NO:	Accession No.	Description	Results*
106	BL00022	EGF-like domain proteins.	BL01187B 12.04 8.500e-11 955-971 BL01187B 12.04 8.500e-11 1092-1108 BL01187B 12.04 9.400e-11 1197-1213 BL01187B 12.04 2.286e-10 302-318 BL01187B 12.04 8.200e-10 1524-1540 BL01187A 9.98 9.143e-10 1338-1350 BL01187A 9.98 9.571e-10 1423-1435 BL01187A 9.98 9.571e-10 1506-1518 BL01187B 12.04 2.125e-09 762-778 BL01187A 9.98 7.000e-09 284-296 BL01187A 9.98 7.000e-09 897-909 BL01187A 9.98 7.000e-09 1179-1191 BL01187A 9.98 8.125e-09 1381-1393 BL00022B 7.54 1.000e-09 924-931 BL00022A 7.48 9.000e-09 194-201
107	BL00649	G-protein coupled receptors family 2 proteins.	BL00649G 13.52 4.194e-13 102-128
107	PR00249	SECRETIN-LIKE GPCR SUPERFAMILY SIGNATURE	PR00249E 14.90 6.958e-09 20-46
107	BL00890	ABC-2 type transport system integral membrane proteins signat.	BL00890A 12.19 1.000e-08 17-28
108	BL00615	C-type lectin domain proteins.	BL00615B 12.25 9.400e-12 163-177
108	PD02205	POLYPROTEIN GLYCOPROTEIN M PRECURSOR CONTAINS:	PD02205O 15.72 7.140e-09 163-195
109	BL01208	VWFC domain proteins.	BL01208B 15.83 1.000e-13 443-458 BL01208B 15.83 1.000e-12 377-392
109	BL00222	Insulin-like growth factor binding proteins.	BL00222B 11.09 1.333e-09 58-74
110	DM01688	2 POLY-IG RECEPTOR.	DM01688G 16.45 8.372e-10 84-116
111	DM01688	2 POLY-IG RECEPTOR.	DM01688G 16.45 8.372e-10 81-113
112	BL00237	G-protein coupled receptors proteins.	BL00237A 27.68 6.211e-23 104-144 BL00237C 13.19 4.115e-13 240-267 BL00237D 11.23 5.286e-13 297-314
112	PR00237	RHODOPSIN-LIKE GPCR SUPERFAMILY SIGNATURE	PR00237G 19.63 5.680e-15 287-314 PR00237A 11.48 4.706e-14 40-65 PR00237B 13.50 9.550e-14 73-95 PR00237F 13.57 9.609e-14 245-270 PR00237C 15.69 7.300e-11 118-141 PR00237E 13.03 1.000e-10 202-226
112	PR00425	BRADYKININ RECEPTOR SIGNATURE	PR00425C 13.23 5.759e-09 104-124
115	PF01140	Matrix protein (MA), p15.	PF01140D 15.54 1.209e-09 845-880
115	DM00215	PROLINE-RICH PROTEIN 3.	DM00215 19.43 4.717e-13 510-543 DM00215 19.43 5.941e-11 494-527 DM00215 19.43 1.000e-10 501-534 DM00215 19.43 4.857e-10

SEQ ID NO:	Accession No.	Description	Results*
			511-544 DM00215 19.43 9.357e-10 627-660 DM00215 19.43 9.518e-10 506-539 DM00215 19.43 1.610e-09 508-541 DM00215 19.43 1.610e-09 515-548 DM00215 19.43 2.831e-09 499-532 DM00215 19.43 4.356e-09 640-673
115	PR00211	GLUTELIN SIGNATURE	PR00211B 0.86 6.417e-09 513-534
115	PR00546	THYROID HORMONE RECEPTOR SIGNATURE	PR00546D 9.44 6.444e-09 848-867
115	PD02059	CORE POLYPROTEIN PROTEIN GAG CONTAINS: P.	PD02059B 24.48 6.958e-09 636-671
115	PR00049	WILM'S TUMOUR PROTEIN SIGNATURE	PR00049D 0.00 8.639e-11 511-526 PR00049D 0.00 8.714e-11 508-523 PR00049D 0.00 1.643e-10 512-527 PR00049D 0.00 8.857e-10 643-658 PR00049D 0.00 2.678e-09 644-659 PR00049D 0.00 5.271e-09 510-525 PR00049D 0.00 6.949e-09 645-660 PR00049D 0.00 7.254e-09 646-661
115	PD00078	REPEAT PROTEIN ANK NUCLEAR ANKYR.	PD00078B 13.14 8.435e-09 293-306
115	PF00023	Ank repeat proteins.	PF00023A 16.03 3.625e-10 132-148 PF00023A 16.03 6.786e-09 300-316 PF00023A 16.03 8.393e-09 200-216 PF00023A 16.03 9.357e-09 40-56 PF00023A 16.03 1.000e-08 166-182
116	PF01140	Matrix protein (MA), p15.	PF01140D 15.54 1.209e-09 787-822
116	DM00215	PROLINE-RICH PROTEIN 3.	DM00215 19.43 4.717e-13 452-485 DM00215 19.43 5.941e-11 436-469 DM00215 19.43 1.000e-10 443-476 DM00215 19.43 4.857e-10 453-486 DM00215 19.43 9.357e-10 569-602 DM00215 19.43 9.518e-10 448-481 DM00215 19.43 1.610e-09 450-483 DM00215 19.43 1.610e-09 457-490 DM00215 19.43 2.831e-09 441-474 DM00215 19.43 4.356e-09 582-615
116	PR00211	GLUTELIN SIGNATURE	PR00211B 0.86 6.417e-09 455-476
116	PR00546	THYROID HORMONE RECEPTOR SIGNATURE	PR00546D 9.44 6.444e-09 790-809
116	PD02059	CORE POLYPROTEIN PROTEIN GAG CONTAINS: P.	PD02059B 24.48 6.958e-09 578-613
116	PR00049	WILM'S TUMOUR PROTEIN SIGNATURE	PR00049D 0.00 8.639e-11 453-468 PR00049D 0.00 8.714e-11 450-465 PR00049D 0.00 1.643e-10 454-469 PR00049D 0.00 8.857e-10 585-600 PR00049D 0.00 2.678e-09 586-601 PR00049D 0.00 5.271e-09 452-467 PR00049D 0.00 6.949e-09 587-602 PR00049D 0.00 7.254e-09 588-603

SEQ ID	Accession	Description	Results*
NO:	No.		
116	PD00078	REPEAT PROTEIN ANK NUCLEAR ANKYR.	PD00078B 13.14 8.435e-09 293-306
116	PF00023	Ank repeat proteins.	PF00023A 16.03 3.625e-10 132-148 PF00023A 16.03 6.786e-09 300-316 PF00023A 16.03 8.393e-09 200-216 PF00023A 16.03 9.357e-09 40-56 PF00023A 16.03 1.000e-08 166-182
119	PR00830	ENDOPEPTIDASE LA (LON) SERINE PROTEASE (S16) SIGNATURE	PR00830A 8.41 6.286e-11 441-461
119	PR00300	ATP-DEPENDENT CLP PROTEASE ATP- BINDING SUBUNIT SIGNATURE	PR00300A 9.56 8.859e-10 437-456
119	PR00819	CBXX/CFQX SUPERFAMILY SIGNATURE	PR00819B 10.83 8.875e-10 436-452
119	BL00113	Adenylate kinase proteins.	BL00113A 12.74 6.262e-09 438-455
119	PR00918	CALICIVIRUS NON- STRUCTURAL POLYPROTEIN FAMILY SIGNATURE	PR00918A 13.76 7.341e-09 431-452
119	BL00674	AAA-protein family proteins.	BL00674C 22.60 5.696e-24 467-510 BL00674D 23.41 8.740e-18 525-572 BL00674B 4.46 1.000e-17 434-456 BL00674E 15.24 3.571e-10 602-622 BL00674A 16.91 8.826e-09 400-421
119	BL01128	Shikimate kinase proteins.	BL01128A 18.84 8.953e-09 437-471
120	PR00705	PAPAIN CYSTEINE PROTEASE (C1) FAMILY SIGNATURE	PR00705A 10.55 4.000e-21 132-148 PR00705B 10.22 2.385e-10 276-287
120	BL00139	Eukaryotic thiol (cysteine) proteases cysteine proteins.	BL00139D 9.24 1.818e-18 295-312 BL00139A 10.29 1.000e-14 132-142 BL00139C 9.23 2.800e-10 275-285
120	PR00704	CALPAIN CYSTEINE PROTEASE (C2) FAMILY SIGNATURE	PR00704C 11.88 6.162e-09 132-149
121	PR00360	C2 DOMAIN SIGNATURE	PR00360B 13.61 8.636e-11 715-729
121	PR00390	PHOSPHOLIPASE C SIGNATURE	PR00390A 15.09 5.390e-20 342-361 PR00390E 14.63 9.357e-20 608-627 PR00390D 15.76 3.250e-17 587-609 PR00390C 12.52 5.714e-14 471-489 PR00390B 12.57 1.269e-11 373-394 PR00390F 12.03 5.333e-10 758-769
121	PF01140	Matrix protein (MA), p15.	PF01140D 15.54 8.535e-09 498-533
121	BL50007	Phosphatidylinositol- specific phospholipase X-box domain proteins	BL50007D 19.54 7.698e-35 582-624 BL50007B 20.90 6.571e-30 407-445 BL50007A 19.61 4.671e-21 343-389

SEQ ID NO:	Accession No.	Description	Results*
		prof.	BL50007E 25.63 7.585e-20 744-781 BL50007C 8.97 4.522e-14 472-489 BL50007A 19.61 8.946e-09 348-394
123	PR00336	LYSOSOME- ASSOCIATED MEMBRANE GLYCOPROTEIN SIGNATURE	PR00336D 9.96 2.393e-09 29-52
126	PR00237	RHODOPSIN-LIKE GPCR SUPERFAMILY SIGNATURE	PR00237E 13.03 6.400e-12 76-100 PR00237D 8.94 1.450e-11 26-48
126	BL00237	G-protein coupled receptors proteins.	BL00237B 5.28 9.182e-09 84-96
127	PR00749	LYSOZYME G SIGNATURE	PR00749C 7.26 4.600e-16 84-103 PR00749F 13.63 2.364e-13 157-174 PR00749D 13.61 1.222e-12 103-124 PR00749E 18.92 5.061e-10 124-143 PR00749B 16.54 6.589e-09 60-82 PR00749H 8.22 7.368e-09 191-212
129	PF00094	von Willebrand factor type D domain proteins.	PF00094B 10.43 3.935e-18 596-614 PF00094B 10.43 8.286e-14 1060-1078
129	PD02576	PRECURSOR GLYCOPROTEIN SIGNAL CELL.	PD02576A 27.60 6.118e-34 894-943 PD02576A 27.60 9.182e-25 424-473 PD02576A 27.60 8.147e-10 791-840
129	BL01253	Type I fibronectin domain proteins.	BL01253G 11.34 8.989e-09 1151-1165
130	BL00243	Integrins beta chain cysteine-rich domain proteins.	BL00243H 17.53 4.375e-10 1190-1216
130	PR00011	TYPE III EGF-LIKE SIGNATURE	PR00011D 14.03 3.508e-11 1195-1214 PR00011B 13.08 4.522e-10 1195-1214 PR00011A 14.06 2.479e-09 1195-1214
130	DM00191	w SPAC8A4.04C RESISTANCE SPAC8A4.05C DAUNORUBICIN.	DM00191D 13.94 6.009e-09 438-477
130	BL00115	Eukaryotic RNA polymerase II heptapeptide repeat proteins.	BL00115Z 3.12 7.485e-09 232-281
130	PF00624	Flocculin repeat proteins.	PF00624J 6.21 9.782e-10 256-311 PF00624F 11.04 1.218e-09 726-762 PF00624G 10.91 3.032e-09 69-124 PF00624J 6.21 4.488e-09 257-312 PF00624J 6.21 6.512e-09 633-688 PF00624J 6.21 7.279e-09 270-325 PF00624G 10.91 8.476e-09 643-698 PF00624J 6.21 8.744e-09 161-216 PF00624J 6.21 9.233e-09 74-129
130	PF00997	Kappa casein.	PF00997D 9.95 9.894e-09 136-171
131	BL00615	C-type lectin domain proteins.	BL00615A 16.68 7.231e-16 195-213 BL00615B 12.25 7.750e-13 294-308
131	PR00356	TYPE II ANTIFREEZE PROTEIN SIGNATURE	PR00356B 14.85 2.648e-09 195-213
132	PR00343	SELECTIN	PR00343C 16.85 4.906e-12 10-29 PR00343C

SEQ ID NO:	Accession No.	Description	Results*
		SUPERFAMILY COMPLEMENT- BINDING REPEAT SIGNATURE	16.85 4.098e-10 125-144 PR00343C 16.85 5.636e-09 68-87 PR00343C 16.85 7.818e-09 418-437
132	PF00084	Sushi domain proteins (SCR repeat proteins.	PF00084B 9.45 7.188e-10 351-363 PF00084B 9.45 5.950e-09 59-71 PF00084C 11.25 7.353e-09 199-209 PF00084B 9.45 7.750e-09 174-186 PF00084C 11.25 9.471e-09 434-444
134	PD00126	PROTEIN REPEAT DOMAIN TPR NUCLEA.	PD00126A 22.53 8.615e-10 456-477
138	BL00132	Zinc carboxypeptidases, zinc-binding region 1 proteins.	BL00132C 21.35 2.552e-35 25-66 BL00132E 17.72 8.333e-27 95-122 BL00132F 13.26 2.500e-24 123-145 BL00132D 12.70 7.000e-18 69-84 BL00132G 10.94 8.594e-17 180-198
138	PR00765	CARBOXYPEPTIDAS E A METALLOPROTEAS E (M14) FAMILY SIGNATURE	PR00765D 14.16 1.857e-14 128-142 PR00765C 12.55 1.667e-11 75-84
139	PD00078	REPEAT PROTEIN ANK NUCLEAR ANKYR.	PD00078B 13.14 2.800e-12 493-506 PD00078B 13.14 6.400e-10 460-473
139	PF00791	Domain present in ZO- 1 and Unc5-like netrin receptors.	PF00791B 28.49 6.417e-10 467-522
139	PF00023	Ank repeat proteins.	PF00023B 14.20 1.818e-09 496-506 PF00023B 14.20 9.182e-09 463-473 PF00023A 16.03 9.679e-09 467-483
142	PR00705	PAPAIN CYSTEINE PROTEASE (C1) FAMILY SIGNATURE	PR00705A 10.55 4.000e-21 132-148 PR00705B 10.22 2.385e-10 276-287
142	BL00139	Eukaryotic thiol (cysteine) proteases cysteine proteins.	BL00139D 9.24 1.818e-18 295-312 BL00139A 10.29 1.000e-14 132-142 BL00139C 9.23 2.800e-10 275-285
142	PR00704	CALPAIN CYSTEINE PROTEASE (C2) FAMILY SIGNATURE	PR00704C 11.88 6.162e-09 132-149
143	BL01019	ADP-ribosylation factors family proteins.	BL01019B 19.49 9.757e-34 106-161 BL01019A 13.20 6.351e-31 62-102 BL01019C 12.52 8.091e-19 165-191
143	BL01020	SAR1 family proteins.	BL01020C 15.35 3.494e-18 90-141
143	PR00328	GTP-BINDING SAR1 PROTEIN SIGNATURE	PR00328A 10.62 4.638e-11 26-50 PR00328C 13.16 4.170e-10 89-115
144	BL50007	Phosphatidylinositol- specific phospholipase X-box domain proteins prof.	BL50007E 25.63 2.761e-18 173-210
144	PR00390	PHOSPHOLIPASE C SIGNATURE	PR00390F 12.03 4.176e-11 187-198
144	PR00399	SYNAPTOTAGMIN SIGNATURE	PR00399D 14.48 4.490e-09 177-188
144	PR00360	C2 DOMAIN	PR00360B 13.61 5.909e-11 144-158

SEQ ID NO:	Accession No.	Description	Results*
		SIGNATURE	PR00360C 8.77 1.321e-09 166-175 PR00360A 14.59 5.500e-09 114-127
149	PR00360	C2 DOMAIN SIGNATURE	PR00360B 13.61 8.636e-11 715-729
149	PR00390	PHOSPHOLIPASE C SIGNATURE	PR00390A 15.09 5.390e-20 342-361 PR00390E 14.63 9.357e-20 608-627 PR00390D 15.76 3.250e-17 587-609 PR00390C 12.52 5.714e-14 471-489 PR00390B 12.57 1.269e-11 373-394 PR00390F 12.03 5.333e-10 758-769
149	PF01140	Matrix protein (MA), p15.	PF01140D 15.54 8.535e-09 498-533
149	BL50007	Phosphatidylinositol- specific phospholipase X-box domain proteins prof.	BL50007D 19.54 7.698e-35 582-624 BL50007B 20.90 6.571e-30 407-445 BL50007A 19.61 4.671e-21 343-389 BL50007E 25.63 7.585e-20 744-781 BL50007C 8.97 4.522e-14 472-489 BL50007A 19.61 8.946e-09 348-394
153	BL00720	Guanine-nucleotide dissociation stimulators CDC25 family sign.	BL00720B 16.57 6.595e-15 996-1020
153	PF00791	Domain present in ZO- 1 and Unc5-like netrin receptors.	PF00791C 20.98 6.011e-12 606-645
153	PD00289	PROTEIN SH3 DOMAIN REPEAT PRESYNA.	PD00289 9.97 5.050e-11 625-639
153	PR00834	HTRA/DEGQ PROTEASE FAMILY SIGNATURE	PR00834F 10.91 2.946e-09 621-634
153	BL00888	Cyclic nucleotide- binding domain proteins.	BL00888B 14.79 4.682e-09 355-379
154	PR00826	FANCONI ANAEMIA GROUP A PROTEIN SIGNATURE	PR00826G 13.17 1.143e-30 1346-1370 PR00826B 11.56 1.150e-29 1123-1146 PR00826A 10.40 1.161e-27 1105-1124 PR00826E 14.92 1.141e-24 1294-1313 PR00826D 6.81 1.132e-23 1253-1272 PR00826F 9.90 1.136e-23 1323-1341 PR00826C 7.00 1.110e-13 1238-1248
154	PR00723	SUBTILISIN SERINE PROTEASE FAMILY (S8) SIGNATURE	PR00723C 10.64 3.340e-09 772-789
155	PR00826	FANCONI ANAEMIA GROUP A PROTEIN SIGNATURE	PR00826G 13.17 1.143e-30 1303-1327 PR00826B 11.56 1.150e-29 1080-1103 PR00826A 10.40 1.161e-27 1062-1081 PR00826E 14.92 1.141e-24 1251-1270 PR00826D 6.81 1.132e-23 1210-1229 PR00826F 9.90 1.136e-23 1280-1298 PR00826C 7.00 1.110e-13 1195-1205
155	PR00723	SUBTILISIN SERINE PROTEASE FAMILY (S8) SIGNATURE	PR00723C 10.64 3.340e-09 772-789
157	PR00267	INTERFERON REGULATORY FACTOR	PR00267D 13.82 3.118e-29 36-59 PR00267C 14.28 4.857e-21 13-31

SEQ ID	Accession	Description	Results*
NO:	No.		
 		SIGNATURE	
157	BL00601	Tryptophan pentad repeat proteins (IRF family) proteins.	BL00601B 20.92 4.500e-31 32-61 BL00601C 19.42 7.429e-09 72-85
159	BL00720	Guanine-nucleotide	BL00720B 16.57 7.677e-17 137-161
		dissociation stimulators CDC25 family sign.	52007202 10.37 7.0770 17 137-101
160	PR00209	ALPHA/BETA GLIADIN FAMILY SIGNATURE	PR00209B 4.88 7.457e-10 1-20
160	PD02699	PROTEIN DNA- BINDING BINDING DNA.	PD02699A 8.91 4.143e-21 144-173 PD02699B 18.28 5.655e-09 173-197
162	BL00232	Cadherins extracellular repeat proteins domain proteins.	BL00232B 32.79 6.671e-15 219-267
163	BL50007	Phosphatidylinositol- specific phospholipase X-box domain proteins prof.	BL50007A 19.61 1.000e-40 675-721 BL50007B 20.90 3.872e-27 734-772 BL50007D 19.54 5.105e-27 1056-1098 BL50007C 8.97 3.935e-14 802-819 BL50007E 25.63 5.661e-14 1217-1254
163	PR00360	C2 DOMAIN SIGNATURE	PR00360B 13.61 4.545e-11 1191-1205
163	PR00390	PHOSPHOLIPASE C SIGNATURE	PR00390B 12.57 5.974e-20 700-721 PR00390A 15.09 6.049e-20 674-693 PR00390E 14.63 7.070e-16 1082-1101 PR00390D 15.76 7.107e-16 1061-1083 PR00390C 12.52 1.000e-13 801-819 PR00390F 12.03 5.500e-09 1231-1242
164	BL00250	TGF-beta family proteins.	BL00250A 21.24 1.500e-31 303-339 BL00250B 27.37 8.200e-30 371-407
164	PR00671	INHIBIN BETA B CHAIN SIGNATURE	PR00671G 5.35 3.250e-27 184-206 PR00671C 4.18 1.173e-26 40-60 PR00671H 13.45 1.000e-25 231-252 PR00671B 4.29 1.474e-25 20-40 PR00671E 8.84 1.115e-23 124-142 PR00671A 8.36 1.429e-22 2-21 PR00671F 13.86 1.105e-21 149-166 PR00671D 3.47 1.100e-20 61-77
164	PR00672	INHIBIN BETA C CHAIN SIGNATURE	PR00672E 10.40 1.419e-10 142-165
164	PR00049	WILM'S TUMOUR PROTEIN SIGNATURE	PR00049D 0.00 3.874e-11 28-43 PR00049D 0.00 9.319e-11 30-45 PR00049D 0.00 9.319e-11 31-46 PR00049D 0.00 2.983e-09 34-49
164	PR00669	INHIBIN ALPHA CHAIN SIGNATURE	PR00669F 5.57 8.483e-09 320-338
164	PR00438	GROWTH FACTOR CYSTINE KNOT SUPERFAMILY SIGNATURE	PR00438A 13.54 1.000e-08 328-338
165	PR00785	NUCLEAR TRANSLOCATOR SIGNATURE	PR00785I 13.44 5.957e-10 284-302
165	BL00038	Myc-type, 'helix-loop- helix' dimerization domain proteins.	BL00038B 16.97 3.930e-09 92-113
166	PR00211	GLUTELIN SIGNATURE	PR00211B 0.86 5.408e-11 268-289 PR00211B 0.86 9.048e-10 274-295 PR00211B 0.86

SEQ ID	Accession	Description	Results*
NO:	No.		
177	7700010		2.167e-09 280-301
166	PR00049	WILM'S TUMOUR PROTEIN SIGNATURE	PR00049D 0.00 7.407e-09 235-250
166	DM00215	PROLINE-RICH PROTEIN 3.	DM00215 19.43 6.186e-09 212-245 DM00215 19.43 6.949e-09 243-276 DM00215 19.43 7.559e-09 227-260 DM00215 19.43 9.085e-09 217-250
167	BL00240	Receptor tyrosine kinase class III proteins.	BL00240F 17.74 2.105e-36 533-581 BL00240E 11.56 5.875e-33 481-519 BL00240D 23.07 9.882e-22 403-458 BL00240C 22.58 8.962e-20 352-401 BL00240G 28.45 4.770e-19 580-633
167	BL00107	Protein kinases ATP- binding region proteins.	BL00107A 18.39 4.938e-21 495-526 BL00107B 13.31 6.400e-15 562-578
167	BL00239	Receptor tyrosine kinase class II proteins.	BL00239E 17.14 9.400e-39 534-584 BL00239F 28.15 2.765e-22 588-633 BL00239B 25.15 6.958e-15 414-462 BL00239C 18.75 3.211e-13 482-505 BL00239D 16.81 9.118e-13 507-533
167	PR00109	TYROSINE KINASE CATALYTIC DOMAIN SIGNATURE	PR00109D 17.04 5.091e-27 563-586 PR00109B 12.27 5.846e-21 495-514 PR00109E 14.41 8.500e-21 607-630 PR00109C 12.85 1.000e-13 544-555 PR00109A 15.00 8.364e-12 443-457
167	BL00790	Receptor tyrosine kinase class V proteins.	BL00790O.7.68 1.889e-17 541-574 BL00790Q 15.61 4.529e-12 599-648 BL00790M 8.74 7.831e-11 486-508 BL00790N 13.25 4.411e-10 508-535
167	BL50001	Src homology 2 (SH2) domain proteins profile.	BL50001B 17.40 2.714e-11 492-513 BL50001D 11.00 5.500e-10 562-573
167	DM00179	w KINASE ALPHA ADHESION T-CELL.	DM00179 13.97 6.211e-10 221-231
167	PD02870	RECEPTOR INTERLEUKIN-1 PRECURSOR.	PD02870D 15.74 9.617e-09 213-248
169	PR00711	ATRIAL NATRIURETIC PEPTIDE SIGNATURE	PR00711A 12.00 9.769e-20 11-30
170	PR00007	COMPLEMENT C1Q DOMAIN SIGNATURE	PR00007A 19.33 1.000e-16 158-185 PR00007C 15.60 8.200e-15 229-251 PR00007B 14.16 5.846e-14 185-205 PR00007D 9.64 5.250e-10 264-275
170	BL01113	C1q domain proteins.	BL01113B 18.26 1.581e-29 164-200 BL01113C 13.18 3.077e-15 229-249 BL01113A 17.99 1.243e-13 50-77 BL01113A 17.99 6.108e-13 35-62 BL01113A 17.99 3.077e-12 41-68 BL01113A 17.99 1.574e-10 38-65 BL01113A 17.99 9.617e-10 44-71 BL01113A 17.99 7.577e-09 59-86 BL01113A 17.99 7.577e-09 110-137
170	BL00420	Speract receptor repeat proteins domain proteins.	BL00420A 20.42 5.154e-12 44-73 BL00420A 20.42 1.655e-11 86-115 BL00420A 20.42 2.328e-10 101-130 BL00420A 20.42 4.185e-09 47-76 BL00420A 20.42 9.031e-09 50-79
171	BL00284	Serpins proteins.	BL00284A 15.64 5.500e-21 26-50
172	PR00749	LYSOZYME G	PR00749C 7.26 4.600e-16 84-103 PR00749F

SEQ ID NO:	Accession No.	Description	Results*
		SIGNATURE	13.63 2.364e-13 157-174 PR00749D 13.61 1.222e-12 103-124 PR00749E 18.92 5.061e-10 124-143 PR00749B 16.54 6.589e-09 60-82 PR00749H 8.22 7.368e-09 191-212
173	PR00678	PI3 KINASE P85 REGULATORY SUBUNIT SIGNATURE	PR00678H 9.13 4.960e-14 406-429
173	PR00049	WILM'S TUMOUR PROTEIN SIGNATURE	PR00049D 0.00 6.748e-11 78-93
173	PR00401	SH2 DOMAIN SIGNATURE	PR00401A 14.00 8.800e-11 400-415
173	PR00239	MOLLUSCAN RHODOPSIN C- TERMINAL TAIL SIGNATURE	PR00239E 1.58 2.518e-10 86-98
173	PR00021	SMALL PROLINE- RICH PROTEIN SIGNATURE	PR00021A 4.31 4.214e-11 181-194 PR00021A 4.31 2.823e-09 180-193 PR00021A 4.31 3.848e-09 182-195 PR00021A 4.31 6.582e-09 183-196 PR00021A 4.31 9.430e-09 178-191 PR00021A 4.31 9.886e-09 179-192
178	PR00343	SELECTIN SUPERFAMILY COMPLEMENT- BINDING REPEAT SIGNATURE	PR00343C 16.85 4.906e-12 10-29 PR00343C 16.85 4.098e-10 125-144 PR00343C 16.85 5.636e-09 68-87 PR00343C 16.85 7.818e-09 418-437
178	PF00084	Sushi domain proteins (SCR repeat proteins.	PF00084B 9.45 7.188e-10 351-363 PF00084B 9.45 5.950e-09 59-71 PF00084C 11.25 7.353e-09 199-209 PF00084B 9.45 7.750e-09 174-186 PF00084C 11.25 9.471e-09 434-444
182	BL01019	ADP-ribosylation factors family proteins.	BL01019B 19.49 5.200e-39 90-145 BL01019A 13.20 1.973e-31 46-86 BL01019C 12.52 1.857e-25 147-173
182	BL01020	SAR1 family proteins.	BL01020C 15.35 7.798e-14 74-125
182	PR00449	TRANSFORMING PROTEIN P21 RAS SIGNATURE	PR00449A 13.20 6.365e-10 17-39
182	PR00440	G-PROTEIN ALPHA SUBUNIT GROUP 12 SIGNATURE	PR00440C 9.54 3.143e-09 62-80
182	PR00328	GTP-BINDING SAR1 PROTEIN SIGNATURE	PR00328A 10.62 5.883e-11 18-42 PR00328C 13.16 5.065e-09 73-99
183	PF00094	von Willebrand factor type D domain proteins.	PF00094B 10.43 3.935e-18 596-614 PF00094B 10.43 8.286e-14 1060-1078
183	PD02576	PRECURSOR GLYCOPROTEIN SIGNAL CELL.	PD02576A 27.60 6.118e-34 894-943 PD02576A 27.60 9.182e-25 424-473 PD02576A 27.60 8.147e-10 791-840
183	BL01253	Type I fibronectin domain proteins.	BL01253G 11.34 8.989e-09 1151-1165
184	BL00243	Integrins beta chain cysteine-rich domain proteins.	BL00243H 17.53 4.375e-10 1190-1216
184	PR00011	TYPE III EGF-LIKE SIGNATURE	PR00011D 14.03 3.508e-11 1195-1214 PR00011B 13.08 4.522e-10 1195-1214

SEQ ID NO:	Accession No.	Description	Results*
			PR00011A 14.06 2.479e-09 1195-1214
184	DM00191	w SPAC8A4.04C RESISTANCE SPAC8A4.05C DAUNORUBICIN.	DM00191D 13.94 6.009e-09 438-477
184	BL00115	Eukaryotic RNA polymerase II heptapeptide repeat proteins.	BL00115Z 3.12 7.485e-09 232-281
184	PF00624	Flocculin repeat proteins.	PF00624J 6.21 9.782e-10 256-311 PF00624F 11.04 1.218e-09 726-762 PF00624G 10.91 3.032e-09 69-124 PF00624J 6.21 4.488e-09 257-312 PF00624J 6.21 6.512e-09 633-688 PF00624J 6.21 7.279e-09 270-325 PF00624G 10.91 8.476e-09 643-698 PF00624J 6.21 8.744e-09 161-216 PF00624J 6.21 9.233e-09 74-129
184	PF00997	Kappa casein.	PF00997D 9.95 9.894e-09 136-171
185	BL00122	Carboxylesterases type- B serine proteins.	BL00122E 22.02 2.862e-20 25-66 BL00122D 12.53 4.000e-11 1-17
186	BL00203	Vertebrate metallothioneins proteins.	BL00203 13.94 8.181e-10 151-197
186	BL00243	Integrins beta chain cysteine-rich domain proteins.	BL00243I 31.77 2.141e-09 8-51
186	PR00451	CHITIN-BINDING DOMAIN SIGNATURE	PR00451A 6.49 5.355e-09 44-53
186	BL00237	G-protein coupled receptors proteins.	BL00237A 27.68 5.592e-09 35-75
186	BL01185	C-terminal cystine knot proteins.	BL01185D 23.45 9.258e-09 50-103
186	BL00246	Wnt-1 family proteins.	BL00246E 20.32 5.553e-09 55-101 BL00246E 20.32 9.788e-09 11-57

^{*} Results include in order: Accession No., subtype, e-value, and amino acid position of the signature in the corresponding polypeptide

TABLE 4

SEQ ID NO:	Pfam Model	Description	E-value	Score	No: of Pfam Domains	Position of the Domain
94	LRR	Leucine Rich Repeat	7.5e-36	132.5	8	58-81:82-105:106- 130:131-154:155- 178:179-202:203- 226:227-250
96	UBX	UBX domain	7e-25	96.1	1	330-409
97	UBX	UBX domain	9.8e-25	95.6	1	299-378
100	AMP- binding	AMP-binding enzyme	2.1e-86	300.5	2	91-230:236-503
101	FG-GAP	FG-GAP repeat	2.2e-07	37.9	1	38-94
102	A2M	Alpha-2- macroglobulin family	1.1e-21	73.0	1	15-152
104	trypsin	Trypsin	3.5e-74	236.2	1	22-240
105	ig	Immunoglobulin	6.3e-24	82.1	3	46-115:148-214:250-

SEQ ID	Pfam	Description	E-value	Score	No: of Pfam	Position of the
NO:	Model				Domains	Domain
	<u> </u>	domain				307
106	EGF	EGF-like domain	3.7e-89	309.6	19	124-151:159- 185:190-217:290- 326:453-488:494- 528:534-570:758- 786:861-897:903- 939:945-979:1082-
						1116:1185- 1221:1302- 1338:1344- 1381:1387- 1423:1429- 1465:1471- 1506:1512-1548
106	ТВ	TB domain	3.5e-65	230.0	6	233-275:341- 372:802-844:994- 1031:1131- 1174:1236-1277
107	7tm_2	7 transmembrane receptor (Secretin family)	0.00044	-68.4	1	2-119
108	lectin_c	Lectin C-type domain	9e-24	92.4	1	52-178
108	Xlink	Extracellular link domain	2.2e-05	13.8	1	47-70
109	vwc	von Willebrand factor type C domain	3.6e-18	73.8	2	337-391:404-457
110	ig	Immunoglobulin domain	2.2e-05	22.4	1	29-106
111	ig	Immunoglobulin domain	2.2e-05	22.4	1	26-103
112	7tm_1	7 transmembrane receptor (rhodopsin family)	5.2e-59	189.6	1	55-305
113	PX	PX domain	1.6e-15	65.0	1	23-164
115	ank	Ank repeat	2e-54	194.2	8	35-67:69-102:127- 160:161-194:195- 228:229-262:263- 295:296-327
115	WH2	WH2 motif	0.0015	25.2	1	703-720
116	ank	Ank repeat	2e-54	194.2	8	35-67:69-102:127- 160:161-194:195- 228:229-262:263- 295:296-327
116	WH2	WH2 motif	0.0015	25.2	1	645-662
119	AAA	ATPase family associated with various cellul	2.8e-71	250.2	1	436-621
120	Peptidase _C1	Papain family cysteine protease	2.3e- 123	412.6	1	114-332
121	PI-PLC-X	Phosphatidylinos itol-specific phospholipase	9.8e-71	248.4	1	338-488
121	PI-PLC-Y	Phosphatidylinos	2.4e-53	190.6	1	532-649

SEQ ID NO:	Pfam Model	Description	E-value	Score	No: of Pfam Domains	Position of the Domain
		itol-specific				
101		phospholipase		<u> </u>	<u> </u>	
121	C2	C2 domain	6.7e-23	89.5	1	667-757
121	PH	PH domain	0.00021	20.7	1	64-172
122	ig	Immunoglobulin domain	0.00088	17.2	1	52-135
123	cNMP_bi nding	Cyclic nucleotide- binding domain	7.9e-15	62.7	1	180-280
124	Sema	Sema domain	3.6e- 118	406.0	1	64-328
126	7tm_1	7 transmembrane receptor (rhodopsin family)	4e-07	24.8	1	1-103
127	SLT	Transglycosylase SLT domain	0.0029	17.5	1	82-202
128	sushi	Sushi domain (SCR repeat)	1.3e-34	128.4	3	29-79:87-140:147- 201
129	vwd	von Willebrand factor type D domain	7.9e- 114	391.6	3	112-260:465- 619:935-1083
129	TIL	Trypsin Inhibitor like cysteine rich domain	7.5e-14	59.5	4	369-425:735- 792:834-895:1204- 1258
131	lectin_c	Lectin C-type domain	2e-46	167.7	1	201-309
132	sushi	Sushi domain (SCR repeat)	1.3e- 106	367.6	10	1-35:40-93:98- 146:155-208:213- 267:272-327:332- 385:390-443:448- 502:507-559
133	RhoGEF	RhoGEF domain	1.7e-18	74.9	1	791-976
133	PDZ	PDZ domain (Also known as DHR or GLGF)	1.5e-09	45.1	1	72-147
133	PH	PH domain	0.00089	18.5	1	1020-1132
134	TPR	TPR Domain	1.2e-16	68.8	6	64-97:107-140:153- 186:263-296:352- 385:449-482
135	PX	PX domain	1.6e-15	65.0	1	23-164
138	Zn_carbO pept	Zinc carboxypeptidase	2.3e- 118	406.6	1	19-227
139	ank	Ank repeat	3.9e-18	73.7	2	462-494:495-527
139	VPS9	Vacuolar sorting protein 9 (VPS9) domain	1.9e-12	54.8	1	264-369
142	Peptidase _C1	Papain family cysteine protease	2.3e- 123	412.6	1	114-332
143	arf	ADP- ribosylation factor family	1.5e-43	158.1	1	8-197
143	ras	Ras family	0.00027	-88.1	1	27-208
144	C2	C2 domain	2.3e-30	114.3	1	96-186
144	PI-PLC-Y	Phosphatidylinos itol-specific	7.6e-14	53.7	1	42-76

SEQ ID NO:	Pfam Model	Description	E-value	Score	No: of Pfam Domains	Position of the Domain
		phospholipase		T		
147	zf-CCCH	Zinc finger C- x8-C-x5-C-x3-H type	4.5e-06	33.6	1	13-39
147	rrm	RNA recognition motif.	0.014	22.0	1	32-103
148	zf-CCCH	Zinc finger C- x8-C-x5-C-x3-H type	3.4e-06	34.0	1	13-39
148	rrm	RNA recognition motif.	0.00011	29.0	1	67-142
149	PI-PLC-X	Phosphatidylinos itol-specific phospholipase	9.8e-71	248.4	1	338-488
149	PI-PLC-Y	Phosphatidylinos itol-specific phospholipase	2.4e-53	190.6	1	532-649
149	C2	C2 domain	6.7e-23	89.5	1	667-757
149	PH	PH domain	0.00021	20.7	1	64-172
153	RasGEF	RasGEF domain	1e-47	172.0	1	907-1092
153	PDZ	PDZ domain (Also known as DHR or GLGF)	5.4e-17	69.9	1	580-661
153	cNMP_bi nding	Cyclic nucleotide- binding domain	3.6e-13	57.2	1	345-435
153	RA	Ras association (RalGDS/AF-6) domain	1.3e-05	32.1	1	799-885
157	IRF	Interferon regulatory factor transcription f	7.6e-43	155.8	1	1-76
159	RasGEF	RasGEF domain	7e-50	179.1	1	47-238
159	PH	PH domain	1.9e-15	59.9	1	390-493
160	RFX_DN A_binding	RFX DNA- binding domain	3.5e-30	113.7	1	95-173
161	rrm	RNA recognition motif.	0.0041	23.8	1	84-157
162	cadherin	Cadherin domain	5.3e-27	103.1	3	27-124:140-227:241- 336
163	PI-PLC-X	Phosphatidylinos itol-specific phospholipase	3.5e-69	243.2	1	670-818
163	PI-PLC-Y	Phosphatidylinos itol-specific phospholipase	9.6e-43	155.4	2	941-954:1031-1123
163	C2	C2 domain	1.8e-08	41.6	1	1148-1230
163	RA	Ras association (RalGDS/AF-6) domain	0.085	3.0	1	1410-1515
164	TGF-beta	Transforming growth factor beta like	1.8e-58	207.7	1	300-407
164	TGFb_pro peptide	TGF-beta propeptide	1.1e-40	148.5	1	62-280
165	PAS	PAS domain	1.3e-07	33.3	2	140-192:294-337

SEQ ID NO:	Pfam Model	Description	E-value	Score	No: of Pfam Domains	Position of the Domain
166	rrm	RNA recognition motif.	9.4e-08	39.2	1	84-157
167	pkinase	Protein kinase domain	3.1e-89	309.9	1	360-636
167	ig	Immunoglobulin domain	3.7e-20	70.0	3	54-111:169-230:268- 289
170	Clq	Clq domain	1.3e-40	148.4	1	149-273
170	Collagen	Collagen triple helix repeat (20 copies)	6.9e-08	39.6	2	20-79:80-139
171	serpin	Serpin (serine protease inhibitor)	2.4e-50	172.8	1	1-145
172	SLT	Transglycosylase SLT domain	0.0029	17.5	1	82-202
173	SH2	SH2 domain	2.4e-16	50.8	I	400-453
178	sushi	Sushi domain (SCR repeat)	1.3e- 106	367.6	10	1-35:40-93:98- 146:155-208:213- 267:272-327:332- 385:390-443:448- 502:507-559
178	EGF	EGF-like domain	7.8e-15	62.7	3	559-590:595- 622:627-654
185	COesteras e	Carboxylesterase	6e-27	94.9	1	3-56

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19.B	Chain	Start	End	PSI- BLAST	Verify	PMF	SeqFold	Coumpound	PDB annotation
	1		5	WEATON.	2000	2000	21020		
i	Ą	09	249	6.5e-22	0.29	-0.02		RIBONUCLEASE INHIBITOR; CHAIN:	COMPLEX (INHIBITOR/NUCLEASE),
								A, D; ANGIOGENIN;	COMPLEX (RI-ANG), HYDROLASE 2
_				-				CRAIN: B, E;	MOLECOLAR RECOGNITION, EPITOPE MAPPING, LEUCINE-RICH
									3 REPEATS
la9n	Y	126	242	1.3e-20	15.0	0.15		U2 RNA HAIRPIN IV;	COMPLEX (NUCLEAR
								CHAIN: Q, R; U2 A';	PROTEIN/RNA) COMPLEX
								CHAIN: A, C; U2 B";	(NUCLEAR PROTEIN/RNA), RNA,
								CHAIN: B, D;	SNRNP, RIBONUCLEOPROTEIN
la9n	Ą	191	249	1e-10	0.25	0.19		U2 RNA HAIRPIN IV;	COMPLEX (NUCLEAR
								CHAIN: Q, R; U2 A';	PROTEIN/RNA) COMPLEX
								CHAIN: A, C; U2 B";	(NUCLEAR PROTEIN/RNA), RNA,
								CHAIN: B, D;	SNRNP, RIBONUCLEOPROTEIN
la9n	Ą	09	207	1.3e-18	0.43	96.0		U2 RNA HAIRPIN IV;	COMPLEX (NUCLEAR
		•						CHAIN: Q, R; U2 A';	PROTEIN/RNA) COMPLEX
								CHAIN: A, C; U2 B";	(NUCLEAR PROTEIN/RNA), RNA,
								CHAIN: B, D;	SNRNP, RIBONUCLEOPROTEIN
la9n	A	88	231	3.9e-22	0.72	98.0		U2 RNA HAIRPIN IV;	COMPLEX (NUCLEAR
				•			'	CHAIN: Q, R; U2 A';	PROTEIN/RNA) COMPLEX
								CHAIN: A, C; U2 B";	(NUCLEAR PROTEIN/RNA), RNA,
								CHAIN: B, D;	SNRNP, RIBONUCLEOPROTEIN
la9n	၁	126	242	1.3e-20	09.0	0.40		U2 RNA HAIRPIN IV;	COMPLEX (NUCLEAR
								CHAIN: Q, R; U2 A';	PROTEIN/RNA) COMPLEX
								CHAIN: A, C; U2 B";	(NUCLEAR PROTEIN/RNA), RNA,
								CHAIN: B, D;	SNRNP, RIBONUCLEOPROTEIN
la9n	၁	09	207	2.6e-18	0.39	0.72		U2 RNA HAIRPIN IV;	COMPLEX (NUCLEAR
								CHAIN: Q, R; U2 A';	PROTEIN/RNA) COMPLEX
-								CHAIN: A, C; U2 B";	(NUCLEAR PROTEIN/RNA), RNA,
٦								CHAIN: B, D;	SNRNP, RIBONUCLEOPROTEIN
la9n	၁	88	231	1.3e-22	0.74	0.77		U2 RNA HAIRPIN IV;	COMPLEX (NUCLEAR

PDB annotation	PROTEIN/RNA) COMPLEX (NUCLEAR PROTEIN/RNA), RNA, SNRNP, RIBONUCLEOPROTEIN	LIGASE CYCLIN A/CDK2- ASSOCIATED PROTEIN P45; CYCLIN A/CDK2-ASSOCIATED PROTEIN P19; SKP1, SKP2, F-BOX, LRR, LEUCINE- RICH REPEAT, SCF, UBIQUITIN, 2 E3, UBIQUITIN PROTEIN LIGASE	LIGASE CYCLIN A/CDK2- ASSOCIATED P45; CYCLIN A/CDK2- ASSOCIATED P19; SKP1, SKP2, F- BOX, LRRS, LEUCINE-RICH REPEATS, SCF, 2 UBIQUITIN, B3, UBIQUITIN PROTEIN LIGASE	COMPLEX (IMMUNOGLOBULIN/HYDROLASE) COMPLEX (IMMUNOGLOBULIN/HYDROLASE), IMMUNOGLOBULIN V 2 REGION, SIGNAL, HYDROLASE, GLYCOSIDASE, BACTERIOLYTIC 3 ENZYME, EGG WHITE COMPLEX (IMMUNOGLOBULIN/HYDROLASE), IMMUNOGLOBULIN/HYDROLASE), ENZYME, EGG WHITE	
Coumpound	CHAIN: Q, R; U2 A'; CHAIN: A, C; U2 B"; CHAIN: B, D;	SKP2; CHAIN: A, C, E, G, I, K, M, O; SKP1; CHAIN: B, D, F, H, J, L, N, P;	SKP2; CHAIN: A, C; SKP1; CHAIN: B, D;	MONOCLONAL ANTIBODY D1.3; CHAIN: A, B; LYSOZYME; CHAIN: C; MONOCLONAL ANTIBODY D1.3; CHAIN: A, B; LYSOZYME; CHAIN: C;	
SeqFold Score					
PMF Score	- ''	-0.11	0.10	0.10	
Verify Score		0.17	0.29	-0.84	
PSI- BLAST		3.9e-12	3.9e-19	0.0065	
End AA		249	239	74	
Start AA		64	09	40	
Chafn The Chaff		<	4	Д	
PDB ID		1fqv	162	1a2y 1a2y	
SEQ SO B		94	<u>4</u> 6	96	

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PDB annotation	PEPTIDE SYNTHETASE GRSA; PEPTIDE SYNTHETASE, GRSA, ADENYLATE FORMING	PEPTIDE SYNTHETASE GRSA; PEPTIDE SYNTHETASE, GRSA, ADENYLATE FORMING	OXIDOREDUCTASE OXIDOREDUCTASE, MONOOXYGENASE, PHOTOPROTEIN, LUMINESCENCE	OXIDOREDUCTASE OXIDOREDUCTASE, MONOOXYGENASE, PHOTOPROTEIN, LUMINESCENCE	COMPLEMENT COMPLEMENT, C3, C3D, ALPHA-ALPHA BARREL	IMMUNE SYSTEM ALPHA-ALPHA BARREL, COMPLEMENT	SERINE PROTEASE SERINE PROTEINASE, TRYPSIN, HYDROLASE	SERINE PROTEASE SERINE PROTEINASE, TRYPSIN, HYDROLASE	SERINE PROTEINASE TRYPSIN-LIKE SERINE PROTEINASE, TETRAMER, HEPARIN, ALLERGY, 2 ASTHMA	COMPLEX (SERINE
Coumpound	GRAMICIDIN SYNTHETASE 1; CHAIN: A, B; PHENYLALANINE; CHAIN: C, D;	GRAMICIDIN SYNTHETASE 1; CHAIN: A, B; PHENYLALANINE; CHAIN: C, D;	LUCIFERASE; CHAIN: NULL;	LUCIFERASE; CHAIN: NULL;	C3D; CHAIN: NULL;	COMPLEMENT C3DG; CHAIN: A;	TRYPSIN; CHAIN: A, B, C, D;	TRYPSIN; CHAIN: A, B, C, D;	BETA-TRYPTASE; CHAIN: A, B, C, D;	ALPHA-THROMBIN;
SeqFold Score	154.59		186.29				210.73		137.52	137.36
PMF Score		1.00		1.00	0.31	0.23		1.00		
Verify Score		0.51		0.78	-0.41	-0.06		0.83		
PSI- BLAST	0	0	0	0	5.1e-20	5.1e-19	1.7e-98	1.7e-98	1.7e-76	1e-69
End AA	579	578	577	576	50	49	247	248	253	254
Start AA	37	20	41	50	1	1	22	22	22	22
Chain ID	∢	∢				A	A	A	∀	Н
PDB	lamu	lamu	1]ci	llci	lc3d	1qqf	1a0j	1a0j	1201	1aht
S B S	100	100	100	100	102	102	104	104	104	104

PDB annotation	PROTEINASE/INHIBITOR)	SERINE PROTEASE HYDROLASE, SERINE PROTEASE	SERINE PROTEASE PRORENIN	EPIDERMAL GLANDULAR KALLIKREIN, SERINE PROTEASE, PROTEIN MATURATION	COMPLEX (BLOOD	COAGULATION/INHIBITOR) AUTOPROTHROMBIN IIA;	HYDROLASE, SERINE	PROTEINASE), PLASMA CALCIUM	BINDLING, 2 GLY COPROTEIN, COMPLEX (BLOOD	COAGULATION/INHIBITOR)	SERINE PROTEASE SERINE	PROTEASE, HYDROLASE,	COMPLEMENT, FACTOR D,	CATALYTIC 2 TRIAD, SELF- REGULATION	BLOOD CLOTTING TSV-PA;	FIBRINOLYSIS, PLASMINOGEN	ACIIVATUR, SEKINE PRUTEINASE,	2 SNAKE VENOM, COMPLEX	(HYDROLASE/INHIBITOR), BLOOD	CLOTTING	SERINE PROTEASE PPE; SERINE	SERINE PROTEASE HYDROLASE,
Coumpound	1AHT 4 CHAIN: L, H; 1AHT 5 HIRUGEN; 1AHT 8 CHAIN: I; 1AHT 9	ALPHA TRYPSIN; CHAIN: A, B;	GLANDULAR	CHAIN: A, B;	ACTIVATED	PROTEIN C; CHAIN: C, L; D-PHE-PRO-	MAI; CHAIN: P;				COMPLEMENT	FACTOR D; CHAIN:	NULL;		PLASMINOGEN	ACIIVATOR;	CHAIN: A, B; GLU-	GLY-ARG-	CHLOROMETHYLKE	TONE INHIBITOR;	ELASTASE; CHAIN:	r, TRYPSIN; CHAIN:
SeqFold Score			193.53		146.28						161.35				190.92						148.11	208.46
PMF Score		1.00																				
Verify Score		0.16																				
PSI- BLAST		3.9e-33	1.7e-82		1e-69						1.3e-76				8.5e-83						3.4e-85	3.4e-95
End		236	253		252						236				253					-	249	253
Start AA	•	154	22		22						22				22						22	22
Chain ID		В	¥		ပ										Ą			•			Ъ	
EDB CD		1aks	1ao5	•	laut						1bio				1bqy						Ibru	1dpo
SEQ NO.		104	104		104						104				104						104	104

	T			1	1	
PDB annotation	SERINE PROTEASE, DIGESTION, PANCREAS, ZYMOGEN, 2 SIGNAL, MULTIGENE FAMILY	COMPLEX (PROTEASEJNHIBITOR) TRYPSIN, COAGULATION FACTOR XA, CHIMERA, PROTEASE, PPACK, 2 CHLOROMETHYLKETONE, COMPLEX (PROTEASE/INHIBITOR)	COMPLEX (PROTEASE/INHIBITOR) TRYPSIN, COAGULATION FACTOR XA, CHIMERA, PROTEASE, PPACK, 2 CHLOROMETHYLKETONE, COMPLEX (PROTEASE/INHIBITOR)			
Coumpound	NULL;	COAGULATION FACTOR XA- TRYPSIN CHIMERA; CHAIN: A; D-PHE- PRO-ARG- CHLOROMETHYLKE TONE (PPACK) WITH CHAIN: I;	COAGULATION FACTOR XA- TRYPSIN CHIMERA; CHAIN: A; D-PHE- PRO-ARG- CHLOROMETHYLKE TONE (PPACK) WITH CHAIN: I;	HYDROLASE (SERINE PROTEINASE) GAMMA- *CHYMOTRYPSIN *A (E.C.3.4.21.1) (\$P*H 7.0) 1GCT 3	COMPLEX(PROTEIN ASE/INHIBITOR) TRYPSIN (E.C.3.4.21.4) COMPLEXED WITH INHIBITOR FROM BITTER 1MCT 3 GOURD 1MCT 4	COMPLEX(PROTEIN
SeqFold Score			189.85	142.82	217.46	
PMF Score		1.00				1.00
Verify Score		0.94				0.95
PSI- BLAST		5.1e-87	5.1e-87	6.8e-76	5.1e-100	5.1e-100
End AA		249	250	249	247	248
Start AA		22	77	12	22	22
Chain D		Ą	A	¥	Ą	Ą
PDB ID		1fxy	1fxy	1gct	lmct	Imct
SEQ NO:		104	104	104	104	10 <u>7</u>

PDB annotation		SERINE PROTEINASE SERINE PROTEINASE, GLYCOPROTEIN	SERINE PROTEINASE SERINE PROTEINASE, GLYCOPROTEIN	COMPLEX (BLOOD COAGULATION/INHIBITOR) CHRISTMAS FACTOR; COMPLEX, INHIBITOR, HEMOPHILIA/EGF,	BLOOD COAGULATION, 2 PLASMA, SERINE PROTEASE, CALCIUM- BINDING, HYDROLASE, 3 GLYCOPROTEIN	GROWTH FACTOR 7S NGF; GROWTH FACTOR (BETA-NGF), HYDROLASE - SERINE PROTEINASE 2 (GAMMA-NGF), INACTIVE SERINE PROTEINASE (ALPHA-NGF)	GROWTH FACTOR 7S NGF; GROWTH FACTOR (BETA-NGF), HYDROLASE - SERINE PROTEINASE 2 (GAMMA-NGF), INACTIVE SERINE PROTEINASE (ALPHA-NGF)	GROWTH FACTOR 7S NGF; GROWTH FACTOR (BETA-NGF), HYDROLASE - SERINE PROTEINASE 2 (GAMMA-NGF), INACTIVE SERINE PROTEINASE (ALPHA-NGF)
Coumpound	ASE/INHIBITOR) TRYPSIN (E.C.3.4.21.4) COMPLEXED WITH INHIBITOR FROM BITTER IMCT 3 GOURD IMCT 4	NEUROPSIN; CHAIN: A, B;	NEUROPSIN; CHAIN: A, B;	FACTOR IXA; CHAIN: C, L.; D-PHE- PRO-ARG; CHAIN: I;		NERVE GROWTH FACTOR; CHAIN: A, B, G, X, Y, Z;	NERVE GROWTH FACTOR; CHAIN: A, B, G, X, Y, Z;	NERVE GROWTH FACTOR; CHAIN: A, B, G, X, Y, Z;
SeqFold Score			233.14	136.25		147.35		204.41
PMF Score		1.00					1.00	
Verify Score		66.0					0.87	
PSI- BLAST		3.4e-87	3.4e-87	1e-77		3.4e-68	3.4e-91	3.4e-91
End		245	252	247		253	248	253
Start AA		22	22	22		31		22
Chain ID		A	A	ပ		«	O	O
PDB ID		lnpm	Inpm	1pfx		lsgf	lsgf	lsgf
SEQ NO:		104	104	104		104	104	104

PDB annotation	COMPLEX (SERINE PROTEASE/INHIBITOR) TRYPSIN INHIBITOR; SERINE PROTEASE, INHIBITOR, COMPLEX, METAL BINDING SITES, 2 PROTEIN ENGINEERING, PROTEASE- SUBSTRATE INTERACTIONS, 3 METALLOPROTEINS	COMPLEX (SERINE PROTEASE/INHIBITOR) TRYPSIN INHIBITOR; SERINE PROTEASE, INHIBITOR, COMPLEX, METAL BINDING SITES, 2 PROTEIN ENGINEERING, PROTEASE. SUBSTRATE INTERACTIONS, 3 METALLOPROTEINS		
Coumpound	ECOTIN; CHAIN: A; ANIONIC TRYPSIN; CHAIN: B;	ECOTIN; CHAIN: A; ANIONIC TRYPSIN; CHAIN: B;	HYDROLASE(SERIN E PROTEINASE) TONIN (E.C. NUMBER NOT ASSIGNED) 1TON 4	HYDROLASE (SERINE PROTEINASE) TRYPSIN (E.C.3.4.21.4) COMPLEXED WITH THE INHIBITOR 1TRN 3 DIISOPROPYL- FLUORIDATE (DFP) 1TRN 4 HUMAN TRYPSIN, DFP
SeqFold Score		198.58	183.92	
PMF Score	1.00			1.00
Verify Score	0.97			98.6
PSI- BLAST	6.8e-95	6.8e-95	6.8e-83	3.4e-98
End	248	253	253	249
Start	22	22	22	22
Chain ID	m	Д		«
PDB D	Islw	lslw	Iton	TI.
ğa Ş	104	104	104	104

PDB annotation		SERINE PROTEASE FACTOR II; SERINE PROTEASE, HYDROLASE, THROMBIN, BLOOD COAGULATION			SERINE PROTEASE HYDROLASE, SERINE PROTEASE, DIGESTION, PANCREAS, 2 ZYMOGEN, SIGNAL	SERINE PROTEASE HYDROLASE,
Coumpound	HYDROLASE (SERINE PROTEINASE) TRYPSIN (E.C.3.4.21.4) COMPLEXED WITH THE INHIBITOR ITRN 3 DIISOPROPYL- FLUORIDATE (DFP) ITRN 4 HUMAN TRYPSIN, DFP	THROMBIN; CHAIN: L, H;	HYDROLASE(SERIN E PROTEINASE) TRYPSIN (E.C.3.4.21.4) COMPLEXED WITH BENZAMIDINE INHIBITOR 2TBS 3	HYDROLASE(SERIN E PROTEINASE) TRYPSIN (E.C.3.4.21.4) COMPLEXED WITH BENZAMIDINE INHIBITOR 2TBS 3	BETA TRYPSIN; CHAIN: NULL;	BETA TRYPSIN;
SeqFold Score	200.17	142.38		205.95	212.27	
PMF			1.00			1.00
Verify Score			0.85			0.90
PSI- BLAST	3.4e-98	3.4e-63	5.1e-94	5.1e-94	8.5e-95	8.5e-95
End AA	250	242	246	254	247	248
Start AA		22	22	22	22	22
Chain ID	٧	Н				
PDB JD	[#]	luvu	2tbs	2tbs	chd5	5ptp
SEQ No.	104	104	104	104	104	104

PDB annotation	SERINE PROTEASE, DIGESTION, PANCREAS, 2 ZYMOGEN, SIGNAL	IMMUNOGLOBULIN IMMUNOGLOBULIN, FAB	COMPLEX (IMMUNOGLOBULIN/AUTOANTIGE N) COMPLEX (IMMUNOGLOBULIN/AUTOANTIGE N), RHEUMATOID FACTOR 2 AUTO- ANTIBODY COMPLEX	IMMUNOGLOBULIN IMMUNOGLOBULIN, ANTIBODY FAB', CATALYST, ALDOLASE REACTION	IMMUNE SYSTEM IMMUNOGLOBULIN; IMMUNOGLOBULIN; ENGINEERING, HUMANIZED AND CHIMERIC ANTIBODY, FAB, 2 X- RAY STRUCTURE, THREE- DIMENSIONAL STRYCTURE, GAMMA- 3 INTERFERON, IMMUNE SYSTEM	IMMUNOGLOBULIN IMMUNOGLOBULIN, KAPPA LIGHT- CHAIN DIMER HEADER	
Coumpound	CHAIN: NULL;	FAB FRAGMENT, ANTIBODY A5B7;	CHAIN: A, B, C, D; IGG4 REA; CHAIN: A; RF-AN IGMLAMBDA; CHAIN: H, L;	IMMUNOGLOBULIN IGG2A; CHAIN: L, H;	ANTIBODY (LIGHT CHAIN); CHAIN: L; ANTIBODY (HEAVY CHAIN); CHAIN: H;	IMMUNOGLOBULIN; CHAIN: A, B;	IMMUNOGLOBULIN FAB' FRAGMENT OF MONOCLONAL ANTIBODY B72.3 1BBJ 3 (MURINE/HUMAN
SeqFold Score			70.41		70.24	66.53	70.26
PMF Score		0.49		0.11			
Verify Score		-0.09		-0.26			
PSI- BLAST		5.1e-20	5.1e-24	1.5e-29	3.4e-19	le-18	1.7e-19
End AA		319	231	226	232	228	228
Start AA		135	35	37	31	31	31
Chain D		A	H	н	H	A	T
PDB TD		lad0	ladq	laxt	1b2w	1b6d	1bbj
S B S		105	105	105	105	105	105

PDB annotation		INSECT IMMUNITY INSECT IMMUNITY, LPS-BINDING,	HOMOPHILIC ADHESION	INSECT IMMUNITY INSECT IMMUNITY, LPS-BINDING, HOMOPHILIC ADHESION	INSECT IMMUNITY INSECT IMMUNITY, LPS-BINDING, HOMOPHILIC ADHESION	COMPLEX (ANTIBODY/PEPTIDE)	POLYSPECIFICITY, CROSS	KEACIIVII Y, FAB-FRAGMENI, PEPTIDE, 2 HIV-1, COMPLEX (ANTIRODY/PEPTIDE)	ANTIBODY THERAPEUTIC	ANTIBODY, CD52				CELL ADHESION NEURAL CELL ADHESION	IMMUNE SYSTEM ABZYME	TRANSITION STATE ANALOG,	IMMUNE SYSTEM			GROWTH FACTOR/GROWTH	MACION RECEPTOR FOR, FOFE,	TRANSDUCTION, 2 DIMERIZATION,
Coumpound	CHIMERA) IBBJ 4	HEMOLIN; CHAIN: A, B;		HEMOLIN; CHAIN: A, B;	HEMOLIN; CHAIN: A, B;	ANTIBODY (CB 4-1);	CHAIN: A, B;	rer IIDE; CHAIN: C;	CAMPATH-	1H:LIGHT CHAIN;	CAMPATH-	1H:HEAVY CHAIN;	CHAIN: H; PEPTIDE ANTIGEN: CHAIN: P.	AXONIN-1; CHAIN: A;	7C8 FAB	FRAGMENT; SHORT	CHAIN; CHAIN: A, C;	/C8 FAB	FRAGMENT; LONG CHAIN; CHAIN: B, D	FIBROBLAST	CHAIN: A, B;	FIBROBLAST
SeqFold Score				105.99		69.73	-		66.53												•	
PMF Score		0.15			0.01									0.07	0.28					60:0	,r.s.	
Verify Score		-0.19			-0.32									-0.09	90'0					-0.19		
PSI- BLAST		1.5e-40		1.5e-40	1e-33	1.7e-19			6.8e-19					1.7e-48	3.4e-31					3.4e-37		
End AA		402		403	312	232		-	228					403	232					322		
Start AA		32		34	4	31			31					32	36					138		
Chain ID		¥		∢	A	¥			L,					V	В					ບ		
PDB ID		1bih		1bih	1bih	1bog			lce1					1cs6	1ct8				-	lcvs		
SEQ NO:		105		105	105	105			105	-				105	105					105		

PDB annotation	GROWTH FACTOR/GROWTH FACTOR RECEPTOR	GROWTH FACTOR/GROWTH FACTOR RECEPTOR FGF, FGFR, IMMUNOGLOBULIN-LIKE, SIGNAL TRANSDUCTION, 2 DIMERIZATION, GROWTH FACTOR/GROWTH FACTOR RECEPTOR	GROWTH FACTOR/GROWTH FACTOR RECEPTOR FGF, FGFR, IMMUNOGLOBULIN-LIKE, SIGNAL TRANSDUCTION, 2 DIMERIZATION, GROWTH FACTOR/GROWTH FACTOR RECEPTOR			VIRUS/VIRAL PROTEIN, RECEPTOR CD155, PVR, HUMAN POLIOVIRUS, ELECTRON MICROSCOPY, 2 POLIOVIRUS-RECEPTOR COMPLEX, VIRUS/VIRAL PROTEIN, RECEPTOR	IMMUNE SYSTEM FC IGG PHAGE DISPLAY PEPTIDE	IMMUNE SYSTEM FCIGG PHAGE
Coumpound	GROWTH FACTOR RECEPTOR 1; CHAIN: C, D;	FIBROBLAST GROWTH FACTOR 2; CHAIN: A, B; FIBROBLAST GROWTH FACTOR RECEPTOR 1; CHAIN: C, D;	FIBROBLAST GROWTH FACTOR 2; CHAIN: A, B; FIBROBLAST GROWTH FACTOR RECEPTOR 1; CHAIN: C, D;	IMMUNOGLOBULIN 3D6 FAB 1DFB 3	IMMUNOGLOBULIN 3D6 FAB 1DFB 3	POLIOVIRUS RECEPTOR; CHAIN: R; VPI; CHAIN: 1; VP2; CHAIN: 2; VP3; CHAIN: 3; VP4; CHAIN: 4;	IMMUNOGLOBULIN LAMBDA HEAVY CHAIN; CHAIN: A, B; ENGINEERED PEPTIDE; CHAIN: E, F;	IMMUNOGLOBULIN
SeqFold Score					67.12			
PMF Score		0.09	0.27	0.28		0.19	0.13	-0.11
Verify Score		-0.07	0.14	-0.19		-0.38	0.08	0.03
PSI- BLAST		8.5e-39	3.46-25	5.1e-20	1.7e-18	6.8e-32	3.46-25	1.7e-50
End AA		322	402	319	232	322	312	404
Start AA		138	243	137	31	33	133	235
Chain		Д	Q	T	T	x	«	A
PDB ED		levs	lcvs	1dfb	1dfb	1dgi	1dn2	1dn2
SEQ EQ EQ		105	105	105	105	105	105	105

PDB annotation	DISPLAY PEPTIDE	COMPLEX, FC FRAGMENT, IGG, FC, COMPLEX, FC FRAGMENT, IGG, FC, RECEPTOR, CD16, GAMMA	COMPLEX CD16; IGG1-FC COMPLEX, FC FRAGMENT, IGG, FC, RECEPTOR, CD16, GAMMA	CELL ADHESION NCAM; NCAM, IMMUNOGLOBULIN FOLD, GLYCOPROTEIN	GROWTH FACTOR/GROWTH FACTOR RECEPTOR FGF2; FGFR2; IMMUNOGLOBULIN (IG)LIKE DOMAINS BELONGING TO THE I- SET 2 SUBGROUP WITHIN IG-LIKE DOMAINS, B-TREFOIL FOLD	GROWTH FACTOR/GROWTH FACTOR RECEPTOR FGF2; FGFR2; IMMUNOGLOBULIN (IG)LIKE DOMAINS BELONGING TO THE I- SET 2 SUBGROUP WITHIN IG-LIKE
Coumpound	LAMBDA HEAVY CHAIN; CHAIN: A, B; ENGINEERED PEPTIDE; CHAIN: E, F;	LOW AFFINITY IMMUNOGLOBULIN GAMMA FC RECEPTOR CHAIN: C; FC FRAGMENT OF HUMAN IGG1; CHAIN: A, B;	LOW AFFINITY IMMUNOGLOBULIN GAMMA FC RECEPTOR CHAIN: C; FC FRAGMENT OF HUMAN IGG1; CHAIN: A, B;	NEURAL CELL ADHESION MOLECULE; CHAIN: A, B, C, D;	FIBROBLAST GROWTH FACTOR 2; CHAIN: A, B, C, D; FIBROBLAST GROWTH FACTOR RECEPTOR 2; CHAIN: E, F, G, H;	FIBROBLÁST GROWTH FACTOR 2; CHAIN: A, B, C, D; FIBROBLAST GROWTH FACTOR
SeqFold Score						
PMF Score		90.0	-0.07	0.99	0.06	0.15
Verify Score		0.11	0.16	0.04	-0.07	0.16
PSI- BLAST		16-24	5.1e-50	2.6e-23	1.5e-34	1.4e-37
End AA		312	404	312	322	326
Start AA		133	235	145	130	138
Chain ID		Ą	¥	Ą	ш	Ð
EDB ED		1e4k	164k	lepf	1ev2	lev2
SEQ NG EL G		105	105	105	105	105

PDB annotation	DOMAINS, B-TREFOIL FOLD			IMMUNE SYSTEM, MEMBRANE PROTEIN CD32; FC RECEPTOR, IMMUNOGLOULIN, LEUKOCYTE, CD32	IMMUNE SYSTEM BET V I-A, BETVI ALLERGEN; BV16 FAB-FRAGMENT, KAPPA MOPC21 CODING SEQUENCE; HEAVY CHAIN OF THE MONOCLONAL ANTIBODY MST2; BET V 1, BV16 FAB FRAGMENT, ANTIBODY ALLERGEN COMPLEX	COMPLEX (HIV ENVELOPE PROTEIN/CD4/FAB) COMPLEX (HIV ENVELOPE PROTEIN/CD4/FAB), HIV-1 EXTERIOR 2 ENVELOPE
Coumpound	RECEPTOR 2; CHAIN: E, F, G, H;	IMMUNOGLOBULIN IMMUNOGLOBULIN FC AND FRAGMENT B OF PROTEIN A COMPLEX 1FC2 4	IMMUNOGLOBULIN IMMUNOGLOBULIN FC AND FRAGMENT B OF PROTEIN A COMPLEX 1FC2 4	FC RECEPTOR FC(GAMMA)RIIA; CHAIN: A;	MAJOR POLLEN ALLERGEN BET V 1- A; CHAIN: A, D, G, J; IMMUNOGLOBULIN KAPPA LIGHT CHAIN; CHAIN: B, E, H, K; ANTIBODY HEAVY CHAIN FAB; CHAIN: C, F, I, L; IMMUNOGLOBULIN FAB FRAGMENT OF HUMANIZED ANTIBODY 4D5, VERSION 4 1FVD 3	ENVELOPE PROTEIN GP120; CHAIN: G; CD4; CHAIN: C; ANTIBODY 17B;
SeqFold Score		66.62			69.02	70.37
PMF Score			0.07	0.42	0.12	
Verify Score			0.04	0.19	-0.14	
PSI- BLAST		1e-24	1e-24	1.3e-22	8.5e-33	3.4e-18
End		322	312	322	232	228
Start AA		128	133	133	33	34
Chain ID		Q	О	A	∪	n
PDB TD		1fc2	1fc2	1fcg	1fsk 1fvd	lgc1
g a g		105	105	105	105	105

PDB annotation	GP120, T-CELL SURFACE GLYCOPROTEIN CD4, 3 ANTIGEN- BINDING FRAGMENT OF HUMAN IMMUNOGLOBULIN 17B, 4 GLYCOSYLATED PROTEIN	IMMUNOGLOBULIN PROTEIN ENGINEERING, ANTIBODY DESIGN, IMMUNOGLOBULIN 2 STRUCTURE, ANTIGEN-BINDING SITE, CANONICAL CONFORMATION, 3 COMPLEMENTARITY- DETERMINING REGION	CATALYTIC ANTIBODY CATALYTIC ANTIBODY 6D9 CATALYTIC ANTIBODY, ESTER HYDROLYSIS, ESTEROLYTIC, FAB,		IMMUNOGLOBULIN INTACT IMMUNOGLOBULIN, V REGION, C REGION, HINGE REGION	IMMUNOGLOBULIN INTACT IMMUNOGLOBULIN, V REGION, C REGION, HINGE REGION
Coumpound	CHAIN: L, H;	ANTIBODY M41; CHAIN: L, H, M, 1;	IMMUNOGLOBULIN 6D9; CHAIN: L, H;	COMPLEX (ANTIBODY/BINDIN G PROTEIN) IGG1 FAB FRAGMENT COMPLEXED WITH PROTEIN G (DOMAIN III) IIGC 5 PROTEIN G, STREPTOCOCCUS	IGG1 INTACT ANTIBODY MAB61.1.3; CHAIN: A, B, C, D	IGGI INTACT ANTIBODY MAB61.1.3; CHAIN: A, B, C, D
SeqFold Score				66.36	72.79	
PMF		0.00	90.0-			0.05
Verify Score	,	-0.06	0.02			-0.25
PSI- BLAST		3.4e-30	1.7e-29	3.4e-16	3.4e-76	3.4e-76
End		231	232	232	403	404
Start AA		36	36	31	19	36
Chain ID		н	н	I _	В	В
PDB ID		1gpo	1hyx	ligc	ligy	ligy
SEQ NO:		105	105	105	105	105

PDB annotation	COMPLEX (IMMUNOGLOBULIN/RECEPTOR) IMMUNOGLOBULIN FOLD, TRANSMEMBRANE, GLYCOPROTEIN, RECEPTOR, 2 SIGNAL, COMPLEX (IMMUNOGLOBULIN/RECEPTOR)	IMMUNOGLOBULIN IMMUNOGLOBULIN, BENCE JONES PROTEIN					
Coumpound	INTERLEUKIN-1 BETA; CHAIN: A; TYPE 1 INTERLEUKIN-1 RECEPTOR; CHAIN: B;	LAMBDA III BENCE JONES PROTEIN CLE; CHAIN: A, B	IMMUNOGLOBULIN ANTIGEN-BINDING FRAGMENT (FAB) (IGG2B, KAPPA) IMAM 3	IMMUNOGLOBULIN IMMUNOGLOBULIN G1 (IGG1) (MCG) WITH A HINGE DELETION IMCO 3	IMMUNOGLOBULIN IMMUNOGLOBULIN G1 (IGG1) (MCG) WITH A HINGE DELETION 1MCO 3	IMMUNOGLOBULIN IMMUNOGLOBULIN G1 (IGG1) (MCG) WITH A HINGE DELETION 1MCO 3	IMMUNOGLOBULIN FAB FRAGMENT (MURINE SE155-4) COMPLEX WITH
SeqFold Score	68.50	69.16		76.87			
PMF Score			0.03	,	0.40	0.07	-0.19
Verlfy Score			-0.23		-0.27	-0.11	0.15
PSI- BLAST	2.6e-27	3.4e-23	6.8e-30	1.5e-82	1.5e-82	1.4e-49	6.8e-15
End AA	326	231	227	404	404	312	404
Start AA	11	34	36	18	32	\$	243
Chain ID	Д	¥.	Ħ	н	н	ж	ı
EDB CI	盘	=	lma m	1mco	lmco	1mco	lmfb
S a S	105	105	105	105	105	105	105

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PDB annotation		IMMUNE SYSTEM MURINE IMMUNOGLOBULIN IGG2A KAPPA, BACTERICIDAL ANTIBODY, 2 EPITOPE P1.16 OF PORA FROM NEISSERIA MENINGITIDIS, 3 UNLIGANDED, IMMUNE SYSTEM	COMPLEX (ANTIBODY/PEPTIDE EPITOPE) ANTIBODY, PEPTIDE ANTIGEN, ANTITUMOR ANTIBODY, 2 COMPLEX (ANTIBODY/PEPTIDE EPITOPE)	IMMUNE SYSTEM CD32; RECEPTOR, FC, CD32, IMMUNE SYSTEM	COMPLEX (ANTIBODY/PEPTIDE) ANTIBODY STRUCTURE, CRYPTOCOCCUS, PEPTIDE, PHAGE LIBRARY, 2 POLYSACCHARIDE, COMPLEX (ANTIBODY/PEPTIDE)	COMPLEX (RT/DNA/FAB) HIV-1 RT; FAB 28; AIDS, HIV-1, RT, POLYMERASE	IMMUNE SYSTEM FAB, ANTIBODY, AROMATASE, P450
Coumpound	HEPTASACCHARIDE 1MFB 3 B: GAL(1- 2)MAN(1-4)RAM(1- 3)GAL(1-2)[ABB(1- 3)]MAN(1-4)RAM 1MFB 4	IGG2A-KAPPA ANTIBODY MN12H2 (LIGHT CHAIN); CHAIN: L; IGG2A- KAPPA ANTIBODY MN12H2 (HEAVY CHAIN); CHAIN: H;	SM3 ANTIBODY; CHAIN: L, H; PEPTIDE EPITOPE; CHAIN: P;	FC GAMMA RIIB; CHAIN: A;	2H1; CHAIN: L, H; PA1; CHAIN: P;	HIV-1 REVERSE TRANSCRIPTASE; CHAIN: A, B; MONOCLONAL ANTIBODY 28; CHAIN: C, D; DNA;	IGGI ANTIBODY 32C2; CHAIN: A;
SeqFold Score					·		
PMF Score	37-7-1	0.16	0.09	0.16	0.03	0.06	90.0
Verify Score		0.03	-0.01	80:0	-0.01	0.06	-0.22
PSI- BLAST		5.1e-29	1.7e-31	2.6e-25	8.5e-29	16-28	3.4e-31
End AA		226	229	325	229	226	226
Start AA		36	33	133		37	33
Chain ID		н	н	«	н	Q	В
PDB ID		1mnu	1sm3	2fcb	2h1p	2hmi	32c2
SEQ NO:		105	105	105	105	105	105

PDB annotation		IMMUNE SYSTEM METAL CHELATASB, CATALYTIC ANTIBODY, FAB FRAGMENT, IMMUNE 2 SYSTEM			EXTRACELLULAR MATRIX FIBRILLIN FRAGMENT, MICROFIBRIL, TB MODULE, MARFAN SYNDROME, 2 CONNECTIVE TISSUE, NOVEL FOLD, EXTRACELLULAR MATRIX EXTRACELLULAR MATRIX	FIBRILLIN FRAGMENT, MICROFIBRIL, TB MODULE,
Coumpound	IGGI ANTIBODY 32C2; CHAIN: B;	METAL CHELATASE CATALYTIC ANTIBODY; CHAIN: A, C; METAL CHELATASE CATALYTIC ANTIBODY; CHAIN: B, D;	IMMUNOGLOBULIN ANTIGEN-BINDING FRAGMENT OF THE MURINE ANTI- PHENYLARSONATE 6FAB 3 ANTIBODY 36-71, FAB 36-71	IMMUNOGLOBULIN FAB FRAGMENT FROM HUMAN IMMUNOGLOBULIN IGGI (LAMBDA, HIL.) 8FAB 3	FIBRILLIN; CHAIN: NULL; FIBRILLIN; CHAIN:	NULL;
SeqFold Score		67.63	70.37	70.63		
PMF Score					96:0	
Verify Score					0.49	
PSI- BLAST		1.46-18	1.7e-16	1.2e-23	2.6e-14 3.9e-16	
End		231	232	226	1284	
Start AA		34	31	34	1221	
Chain ID		∀	ц	∢		
PDB ID		3fet	6fab	8fab	lapj lapj	
SEQ No.		105	105	105	106	

PDB annotation	MARFAN SYNDROME, 2 CONNECTIVE TISSUE, NOVEL FOLD, EXTRACELLULAR MATRIX	EXTRACELLULAR MATRIX FIBRILLIN FRAGMENT, MICROFIBRIL, TB MODULE, MARFAN SYNDROME, 2 CONNECTIVE TISSUE, NOVEL FOLD, EXTRACELLULAR MATRIX	COMPLEMENT COMPLEMENT, EGF, CALCIUM BINDING, SERINE PROTEASE	COMPLEX (BLOOD COAGULATION/INHIBITOR) AUTOPROTHROMBIN IIA; HYDROLASE, SERINE PROTEINASE), PLASMA CALCIUM	BINDING, 2 GLYCOPROTEIN, COMPLEX (BLOOD COAGULATION/INHIBITOR)	COMPLEX (BLOOD COAGULATION/INHIBITOR) AUTOPROTHROMBIN IIA; HYDROLASE, SERINE PROTEINASE), PLASMA CALCIUM BINDING, 2 GLYCOPROTEIN, COMPLEX (BLOOD COAGULATION/INHIBITOR)	COMPLEX (BLOOD COAGULATION/INHIBITOR) AUTOPROTHROMBIN IIA; HYDROLASE, SERINE PROTEINASE), PLASMA CALCIUM BINDING, 2 GLYCOPROTEIN, COMPLEX (BLOOD
Coumpound		FIBRILLIN; CHAIN: NULL;	COMPLEMENT PROTEASE CIR; CHAIN: NULL;	ACTIVATED PROTEIN C; CHAIN: C, L; D-PHE-PRO- MAI; CHAIN: P;		ACTIVATED PROTEIN C; CHAIN: C, L; D-PHE-PRO-MAI; CHAIN: P;	ACTIVATED PROTEIN C; CHAIN: C, L; D-PHE-PRO- MAI; CHAIN: P;
SeqFold Score							
PMF Score		0.55	0.12	0.23		-0.01	0.71
Verify Score		0.31	-0.15	-0.17		0.05	0.48
PSI- BLAST		1.2e-10	1e-10	5.2e-13		5.2e-10	1e-20
End AA		1043	1548	1229		200	1441
Start AA		626	1508	1133		115	1338
Chain ID				н		ı	J.
PDB ID		1 apj	lapq	laut		laut	laut
SEQ No:		106	106	106		106	106

PDB annotation	COAGULATION/INHIBITOR)	COMPLEX (BLOOD COAGULATION/INHIBITOR) AUTOPROTHROMBIN IIA; HYDROLASE, SERINE PROTEINA SEP, DI ASMA CALCITIM	BINDING, 2 GLYCOPROTEIN, COMPLEX (BLOOD COAGULATIONINHIBITOR)	COMPLEX (BLOOD COAGULATION/INHIBITOR) AUTOPROTHROMBIN IIA; HYDROLASE, SERINE	PROTEINASE), PLASMA CALCIUM BINDING, 2 GLYCOPROTBIN, COMPLEX (BLOOD COAGULATION/INHIBITOR)	COMPLEX (BLOOD COAGULATION/INHIBITOR)	AUTOPROTHROMBIN IIA; HYDROLASE, SERINE	PROTEINASE), PLASMA CALCIUM BINDING, 2 GLYCOPROTEIN,	COMPLEX (BLOOD COAGULATION/INHIBITOR)	COMPLEX (BLOOD COAGULATION/INHIBITOR)	AUTOPROTHROMBIN IIA; HYDROLASE, SERINE	PROTEINASE), PLASMA CALCIUM	COMPLEX (BLOOD	COAGULATION/INFIBITOR) COAGULATION/INHIBITOR)
Coumpound		ACTIVATED PROTEIN C; CHAIN: C, L; D-PHE-PRO- MAI; CHAIN: P;		ACTIVATED PROTEIN C; CHAIN: C, L; D-PHE-PRO- MAI; CHAIN: P;		ACTIVATED PROTEIN C; CHAIN:	C, L; D-PHE-PRO- MAI; CHAIN: P;			ACTIVATED PROTEIN C; CHAIN:	C, L; D-PHE-PRO- MAI; CHAIN: P;			ACTIVATED PROTEIN C; CHAIN:
SeqFold Score														
PMF Score		99.0		0.05		0.10				0.74				0.11
Verify Score		0.18		-0.06		0.01				0.14				0.17
PSI- BLAST		2.6e-23		1.2e-15		2.6e-10				2.6e-23				2.6e-14
End AA		1522		1555		290				575				914
Start AA		1423		1449		174				487				816
Chain ID		i i		H		ı,				7				1
PDB U		laut		laut		laut				laut				laut
SE SE		106		106		106				106				106

PDB annotation	AUTOPROTHROMBIN IIA; HYDROLASE, SERINE PROTEINASE), PLASMA CALCIUM BINDING, 2 GLYCOPROTEIN, COMPLEX (BLOOD COAGULATIONINHIBITOR)	COMPLEX (BLOOD COAGULATION/INHIBITOR) AUTOPROTHROMBIN IIA; HYDROLASE, SERINE PROTEINASE), PLASMA CALCIUM BINDING, 2 GLYCOPROTEIN, COMPLEX (BLOOD COAGULATION/INHIBITOR)	COMPLEX (BLOOD COAGULATION/INHIBITOR) AUTOPROTHROMBIN IIA; HYDROLASE, SERINE PROTEINASE), PLASMA CALCIUM BINDING, 2 GLYCOPROTEIN, COMPLEX (BLOOD COAGULATION/INHIBITOR)	BLOOD COAGULATION, SERINE PROTEASE, COMPLEX, CO-FACTOR, 2 RECEPTOR ENZYME, INHIBITOR, GLA, EGF, 3 COMPLEX (SERINE PROTEASE/COFACTOR/LIGAND)	BLOOD COAGULATION, SERINE PROTEASE, COMPLEX, CO-FACTOR, 2 RECEPTOR ENZYME, INHIBITOR,
Coumpound	C, L; D-PHE-PRO- MAI; CHAIN: P;	ACTIVATED PROTEIN C; CHAIN: C, L; D-PHE-PRO- MAI; CHAIN: P;	ACTIVATED PROTEIN C; CHAIN: C, L; D-PHE-PRO- MAI; CHAIN: P;	BLOOD COAGULATION FACTOR VIIA; CHAIN: L, H; SOLUBLE TISSUE FACTOR; CHAIN: T, U; D-PHE-PHE-ARG- CHLOROMETHYLKE TONE (DFFRCMK) WITH CHAIN: C;	BLOOD COAGULATION FACTOR VIIA;
SeqFold Score					
PMF Score		0.27	0.22	-0.18	0.07
Verify Score		0.16	0.26	0.01	-0.05
PSI- BLAST		6.5e-19	9.1e-18	6.8e-12	3.4e-12
End AA		950	286	1124	1230
Start AA		859	897	1039	1137
Chain D		ы	1	L	T
PDB ID		laut	laut	1dan	ldan
SEQ NO:		106	106	106	106

PDB annotation	GLA, EGF, 3 COMPLEX (SERINE PROTBASE/COFACTOR/LIGAND)	BLOOD COAGULATION, SERINE PROTEASE, COMPLEX, CO-FACTOR, 2 RECEPTOR ENZYME, INHIBITOR, GLA, EGF, 3 COMPLEX (SERINE PROTEASE/COFACTOR/LIGAND)	MEMBRANE PROTEIN NMR, THROMBIN, EGF MODULE, ANTICOAGULANT, GLYCOSYLATION	MEMBRANE PROTEIN NMR, THROMBIN, EGF MODULE, ANTICOAGULANT, GLYCOSYLATION	MEMBRANE PROTEIN NMR, THROMBIN, EGF MODULE, ANTICOAGULANT, GLYCOSYLATION	HYDROLASE/HYDROLASE INHIBITOR PROTEIN-PEPTIDE COMPLEX
Coumpound	CHAIN: L, H; SOLUBLE TISSUE FACTOR; CHAIN: T, U; D-PHE-PHE-ARG- CHLOROMETHYLKE TONE (DFFRCMK) WITH CHAIN: C;	BLOOD COAGULATION FACTOR VIIA; CHAIN: L, H; SOLUBLE TISSUE FACTOR; CHAIN: T, U; D-PHE-PHE-ARG- CHLOROMETHYLKE TONE (DFFRCMK) WITH CHAIN: C;	THROMBOMODULI N; CHAIN: A;	THROMBOMODULI N; CHAIN: A;	THROMBOMODULI N; CHAIN: A;	DES-GLA FACTOR VIIA (HEAVY CHAIN); CHAIN: H, I; DES-GLA FACTOR VIIA (LIGHT CHAIN); CHAIN: L, M; (DPN)-
SeqFold Score						
PMF Score		0.04	-0.07	0.10	0.10	-0.18
Verify Score		-0.17	0.30	0.12	0.28	0.16
PSI- BLAST		3.4e-10	1e-19	9.1e-19	5.2e-15	6.8e-12
End		1032	1511	570	981	1124
Start AA		941	1423	488	897	1039
Chain ID		н	A	A	A	ı
PDB DD	·	1dan	1dqb	1dqb	1dqb	1dva
SEQ EQ		106	106	106	106	106

PDB annotation		HYDROLASE/HYDROLASE INHIBITOR PROTEIN-PEPTIDE COMPLEX	HYDROLASE/HYDROLASE INHIBITOR PROTEIN-PEPTIDE COMPLEX	SERINE PROTEINASE COAGULATION FACTOR II; COAGULATION FACTOR II; FETOMODULIN, TM, CD141 ANTIGEN; EGR-CMK SERINE PROTEINASE, EGF-LIKE DOMAINS, ANTICOAGULANT COMPLEX, 2 ANTIFIBRINOLYTIC COMPLEX	SERINE PROTEINASE COAGULATION FACTOR II; COAGULATION FACTOR II;
Coumpound	PHE-ARG; CHAIN: C, D; PEPTIDE B-76; CHAIN: X, Y;	DES-GLA FACTOR VIIA (HEAVY CHAIN); CHAIN: H, I; DES-GLA FACTOR VIIA (LIGHT CHAIN); CHAIN: L, M; (DPN)- PHE-ARG; CHAIN: C, D; PEPTIDE E-76; CHAIN: X, Y;	DES-GLA FACTOR VIIA (HEAVY CHAIN); CHAIN: H, I; DES-GLA FACTOR VIIA (LIGHT CHAIN); CHAIN: L, M; (DPN)- PHE-ARG; CHAIN: C, D; PEPTIDE E-76; CHAIN: X, Y;	THROMBIN LIGHT CHAIN; CHAIN: A, B, C, D; THROMBIN HEAVY CHAIN; CHAIN: M, N, O, P; THROMBOMODULI N; CHAIN: I, J, K, L; THROMBIN INHIBITOR L-GLU-L- GLY-L-ARM; CHAIN: B, F, G, H;	THROMBIN LIGHT CHAIN; CHAIN: A, B, C, D; THROMBIN
SeqFold Score					
PMF Score		-0.05	0.16	0.19	0.11
Verify Score		0.25	-0.29	0.05	0.23
PSI- BLAST		le-13	3.4e-10	3.9e-14	3.9e-12
End		379	1032	1338	217
Start AA		286	941	1181	124
Chain ID		L	L	I	I
PDB ID		1dva	1dva	1dx5	1dx5
SEQ No.		106	106	106	106

	INS,	AINS,	VINS,	
tation	FETOMODULIN, TM, CD141 ANTIGEN; EGR-CMK SERINE PROTEINASE, EGF-LIKE DOMAINS, ANTICOAGULANT COMPLEX, 2 ANTIFIBRINOLYTIC COMPLEX	OR II; OR II; CD141 SERINE KE DOM. OMPLEX,	SERINE PROTEINASE COAGULATION FACTOR II; COAGULATION FACTOR II; FETOMODULIN, TM, CD141 ANTIGEN; EGR-CMK SERINE PROTEINASE, EGF-LIKE DOMAINS, ANTICOAGULANT COMPLEX, 2 ANTIFIBRINOLYTIC COMPLEX	IE CTOR II; CTOR II; I, CD141 K SERINE
PDB annotation	FETOMODULIN, TM, CD141 ANTIGEN; EGR-CMK SERINE PROTEINASE, EGF-LIKE DOM ANTICOAGULANT COMPLEX ANTIFIBRINOLYTIC COMPLE	SERINE PROTEINASE COAGULATION FACTOR II; COAGULATION FACTOR II; FETOMODULIN, TM, CD141 ANTIGEN; EGR-CMK SERINE PROTEINASE, EGF-LIKE DOM, ANTICOAGULANT COMPLEX, ANTIFIBRINOLYTIC COMPLEX	SERINE PROTEINASE COAGULATION FACTOR II; COAGULATION FACTOR II; FETOMODULIN, TM, CD141 ANTIGEN; EGR-CMK SERINE PROTEINASE, EGR-LIKE DON ANTICOAGULANT COMPLEX ANTIFIBRINOLYTIC COMPLEX	SERINE PROTEINASE COAGULATION FACTOR II; COAGULATION FACTOR II; FETOMODULIN, TM, CD141 ANTIGEN; EGR-CMK SERINE
	FETOMOL ANTIGEN, PROTEIN, ANTIFIER	SERINE PI COAGULA COAGULA FETOMOI ANTIGEN PROTEINA ANTIFIBR	SERINE P COAGUL COAGUL FETOMOI ANTIGEN PROTEIN ANTICOA	SERINE P COAGUL COAGUL FETOMO ANTIGEN
pun	IN; (, 0, P; (ODUL) J, K, L; CGLU-L- ; CHAIN:	LIGHT IN: A, B, ABIN AIN; AIN; AODULI J, K, L; L-GLU-L- I; CHAIN:	LIGHT VIN: A, B, MBIN AIN; A'O, P; A'ODULI J, K, L; L-GLU-L- I; CHAIN:	LIGHT AIN: A, B, MBIN AIN; X, O, P;
Coumpound	HEAVY CHAIN; CHAIN: M, N, O, P; THROMBOMODULI N; CHAIN: I, I, K, L; THROMBIN INHIBITOR L-GLU-L- GLY-L-ARM; CHAIN: E, F, G, H;	THROMBIN LIGHT CHAIN; CHAIN: A, B, C, D; THROMBIN HEAVY CHAIN; CHAIN: M, N, O, P; THROMBOMODULI N; CHAIN: I, I, K, L; THROMBIN INHIBITOR L-GLU-L-GLY-L-ARM; CHAIN: E, F, G, H;	THROMBIN LIGHT CHAIN; CHAIN: A, B, C, D; THROMBIN HEAVY CHAIN; CHAIN: M, N, O, P; THROMBOMODULI N; CHAIN: I, J, K, L; THROMBIN INHIBITOR L-GLU-L-GLY-L-ARM; CHAIN: E, F, G, H;	THROMBIN LIGHT CHAIN; CHAIN: A, B, C, D; THROMBIN HEAVY CHAIN; CHAIN: M, N, O, P;
SeqFold Score				
PMF Score		0.12	0.40	0.21
Verify Score		-0.18	-0.33	0.19
PSI- BLAST		7.8e-16	1.36-22	9.1e-27
End AA		1381	1465	1506
Start AA		1266	1340	1383
Chain			Н	Н
PDB ID		1dx5	1dx5	1dx5
SEQ El	2	106	106	106

PDB annotation	PROTEINASE, EGF-LIKE DOMAINS, ANTICOAGULANT COMPLEX, 2 ANTIFIBRINOLYTIC COMPLEX	SERINE PROTEINASE COAGULATION FACTOR II; COAGULATION FACTOR II; FETOMODULIN, TM, CD141 ANTIGEN; EGR-CMK SERINE PROTEINASE, EGF-LIKE DOMAINS, ANTICOAGULANT COMPLEX, 2 ANTIFIBRINOLYTIC COMPLEX	SERINE PROTEINASE COAGULATION FACTOR II; COAGULATION FACTOR II; FETOMODULIN, TM, CD141 ANTIGEN, EGR-CMK SERINE PROTEINASE, EGF-LIKE DOMAINS, ANTICOAGULANT COMPLEX, 2 ANTIFIBRINOLYTIC COMPLEX	SERINE PROTEINASE COAGULATION FACTOR II; COAGULATION FACTOR II; FETOMODULIN, TM, CD141 ANTIGEN; EGR-CMK SERINE PROTEINASE, EGF-LIKE DOMAINS, ANTICOAGULANT COMPLEX, 2
Coumpound	THROMBOMODULI N; CHAIN: I, J, K, L; THROMBIN INHIBITOR L-GLU-L- GLY-L-ARM; CHAIN: B, F, G, H;	THROMBIN LIGHT CHAIN; CHAIN: A, B, C, D; THROMBIN HEAVY CHAIN; CHAIN: M, O, P; THROMBOMODULI N; CHAIN: I, J, K, L; THROMBIN INHIBITOR L-GLU-L- GLY-L-ARM; CHAIN: E, F, G, H;	THROMBIN LIGHT CHAIN; CHAIN: A, B, C, D; THROMBIN HEAVY CHAIN; CHAIN: M, N, O, P; THROMBOMODULI N; CHAIN: I, I, K, L; THROMBIN INHIBITOR L-GLU-L- GLY-L-ARM; CHAIN: E, F, G, H;	THROMBIN LIGHT CHAIN; CHAIN: A, B, C, D; THROMBIN HEAVY CHAIN; CHAIN: M, N, O, P; THROMBOMODULI N; CHAIN: I, I, K, L;
SeqFold Score				
PMF Score		0.88	0.00	0.05
Verify Score		0.32	0.10	0.13
PSI- BLAST		16-23	8.5e-12	1.36-15
End		1548	1598	320
Start AA		1424	1466	185
Chain ID		1	I	П
PDB ID		1dx5	1dx5	1dx5
SEQ NO NO		106	106	106

PDB annotation	ANTIFIBRINOLYTIC COMPLEX	SERINE PROTEINASE COAGULATION FACTOR II; COAGULATION FACTOR II; FETOMODULIN, TM, CD141 ANTIGEN; EGR-CMK SERINE PROTEINASE, EGF-LIKE DOMAINS, ANTICOAGULANT COMPLEX, 2 ANTIFIBRINOLYTIC COMPLEX	SERINE PROTEINASE COAGULATION FACTOR II; COAGULATION FACTOR II; FETOMODULIN, TM, CD141 ANTIGEN; EGR-CMK SERINE PROTEINASE, EGF-LIKE DOMAINS, ANTICOAGULANT COMPLEX, 2 ANTIFIBRINOLYTIC COMPLEX	SERINE PROTEINASE COAGULATION FACTOR II; COAGULATION FACTOR II; FETOMODULIN, TM, CD141 ANTIGEN; EGR-CMK SERINE PROTEINASE, EGF-LIKE DOMAINS, ANTICOAGULANT COMPLEX, 2 ANTIFIBRINOLYTIC COMPLEX
Coumpound	THROMBIN INHIBITOR L-GLU-L- GLY-L-ARM; CHAIN: E, F, G, H;	THROMBIN LIGHT CHAIN; CHAIN: A, B, C, D; THROMBIN HEAVY CHAIN; CHAIN: M, N, O, P; THROMBOMODULI N; CHAIN: I, I, K, L; THROMBIN IHROMBIN INHIBITOR L-GLU-L- GLY-L-ARM; CHAIN: E, F, G, H;	THROMBIN LIGHT CHAIN; CHAIN: A, B, C, D; THROMBIN HEAVY CHAIN; CHAIN: M, N, O, P; THROMBOMODULI N; CHAIN: I, I, K, L; THROMBIN INHIBITOR L-GLU-L- GLY-L-ARM; CHAIN: B, F, G, H;	THROMBIN LIGHT CHAIN; CHAIN: A, B, C, D; THROMBIN HEAVY CHAIN; CHAIN: M, N, O, P; THROMBOMODULI N; CHAIN: I, I, K, L; THROMBIN INHIBITOR L-GLU-L-
SeqFold Score		,		
PMF Score		0.53	-0.13	0.64
Verify Score		0.07	0.19	-0.02
PSI- BLAST		1.3e-23	1.7e-16	1e-23
End AA		570	612	979
Start AA			489	857
Chain D		н	-	H
PDB ID		14x5	14x5	14x5
SEQ B) B) Si		106	106	106

PDB annotation		MATRIX PROTEIN EXTRACELLULAR MATRIX, CALCIUM-BINDING,	GLYCOPROTEIN, 2 REPEAT, SIGNAL, MULTIGENE FAMILY,	DISEASE MUTATION, 3 EGF-LIKE DOMAIN, HUMAN FIBRILLIN-1 FRAGMENT, MATRIX PROTEIN	MATRIX PROTEIN	CALCIUM-BINDING,	GLYCOPROTEIN, 2 REPEAT,	DISEASE MUTATION, 3 EGF-LIKE	DOMAIN, HUMAN FIBRILLIN-1	FRAGMENT, MATRIX PROTEIN	MATRIX PROTEIN EXTRACELLULAR MATRIX	CALCIUM-BINDING,	GLYCOPROTEIN, 2 REPEAT,	SIGNAL, MULTIGENE FAMILY,	DISEASE MUTATION, 3 EGF-LIKE	DOMAIN, HOMAN FIBRULLIN-1 FRAGMENT, MATRIX PROTEIN	MATRIX PROTEIN	EXTRACELLULAR MATRIX,	CALCIUM-BINDING,	GLYCOPROTEIN, 2 REPEAT,	SIGNAL, MULI IGENE FAMILY,	DISEASE MOTATION, 3 EGF-LINE	FRAGMENT, MATRIX PROTEIN	MATRIX PROTEIN
Coumpound	GLY-L-ARM; CHAIN: E, F, G, H;	FIBRULLIN; CHAIN: NULL;			FIBRILLIN; CHAIN:	ויטבר,					FIBRILLIN; CHAIN: NULL:						FIBRILLIN; CHAIN:	NULL;						FIBRILLIN; CHAIN:
SeqFold Score														-										
PMF Score		0.29			86.0						0.78						0.88							0.72
Verify Score		0.05			0.11						-0.33						80.0							0.18
PSI- BLAST		1.7e-12			6.5e-13					,	1e-12						3.9e-19		,					3.9e-19
End AA		1212			1224					3,0,	1265						1402							1527
Start AA		1145			1178						1811						1337							1465
Chain ID								-																
PDB ID		lemn			1emn						lemn						lemn						•	lemn
SEQ B S		106			106						99						106							106

PDB annotation	EXTRACELLULAR MATRIX, CALCIUM-BINDING, GLYCOPROTEIN, 2 REPEAT, SIGNAL, MULTIGENE FAMILY, DISEASE MUTATION, 3 EGF-LIKE DOMAIN, HUMAN FIBRILLIN-1 FRAGMENT, MATRIX PROTEIN	MATRIX PROTEIN EXTRACELLULAR MATRIX, CALCIUM-BINDING, GLYCOPROTEIN, 2 REPEAT, SIGNAL, MULTIGENE FAMILY, DISEASE MUTATION, 3 EGF-LIKE DOMAIN, HUMAN FIBRILLIN-1 FRAGMENT, MATRIX PROTEIN	MATRIX PROTEIN EXTRACELLULAR MATRIX, CALCIUM-BINDING, GLYCOPROTEIN, 2 REPEAT, SIGNAL, MULTIGENE FAMILY, DISEASE MUTATION, 3 EGF-LIKE DOMAIN, HUMAN FIBRILLIN-1 FRAGMENT, MATRIX PROTEIN	MATRIX PROTEIN EXTRACELLULAR MATRIX, CALCIUM-BINDING, GLYCOPROTEIN, 2 REPEAT, SIGNAL, MULTIGENE FAMILY, DISEASE MUTATION, 3 EGF-LIKE DOMAIN, HUMAN FIBRILLIN-1 FRAGMENT, MATRIX PROTEIN	MATRIX PROTEIN EXTRACELLULAR MATRIX, CALCIUM-BINDING, GLYCOPROTEIN, 2 REPEAT,
Coumpound	NULL;	FIBRILLIN; CHAIN: NULL;	FIBRILLIN; CHAIN: NULL;	FIBRILLIN; CHAIN: NULL;	FIBRILLIN; CHAIN: NULL;
SeqFold Score					
PMF		82.0	-0.19	0.62	0.19
Verify Score		0.28	0.05	-0.58	0.12
PSI- BLAST		1.3e-11	3.4e-13	6.5e-20	16-15
End		1551	489	549	615
Start AA		1506	410	88 8	530
Chain					
PDB ID		1emn	lemn	lemn	lemn
SEQ No. ed		106	106	106	106

PDB annotation	SIGNAL, MULTIGENE FAMILY, DISEASE MUTATION, 3 EGF-LIKE DOMAIN, HUMAN FIBRILLIN-1 FRAGMENT, MATRIX PROTEIN		LIPID BINDING PROTEIN LDL RECEPTOR; BETA HAIRPIN, 3-10 N: HELIX, CALCIUM BINDING		BLOOD CLOTTING COMPLEX(SERINE PROTEASE/COFACTOR/LIGAND), BLOOD COAGULATION, 2 SERINE PROTEASE, COMPLEX, CO-FACTOR, RECEPTOR ENZYME, 3 INHIBITOR, GLA, EGF, COMPLEX (SERINE 4 PROTEASE/COFACTOR/LIGAND), BI OOD CI OTTING
Coumpound		FIBRILLIN; CHAIN: NULL;	LOW-DENSITY LIPOPROTEIN RECEPTOR; CHAIN: A;	BLOOD COAGULATION FACTOR VIIA; CHAIN: L; BLOOD COAGULATION FACTOR VIIA; CHAIN: H; SOLUBLE TISSUE FACTOR; CHAIN: T; 51.15; CHAIN: I;	BLOOD COAGULATION FACTOR VIIA; CHAIN: L; BLOOD COAGULATION FACTOR VIIA; CHAIN: H; SOLUBLE TISSUE FACTOR;
SeqFold Score					
PMF Score		0.12	-0.18	-0.18	0.03
Verify Score		-0.64	0.09	0.07	-0.18
PSI- BLAST		6.8e-13	1.7e-10	6.8e-12	3.4e-12
End AA		777	148	1124	1230
Start AA		711	76	1039	1137
Chain ID			¥	LJ.	u
PDB TD		lemn	1 5 5y	lfak	1fak
SEQ No B		106	106	106	106

				, , , , , , , , , , , , , , , , , , , 	
PDB annotation		BLOOD CLOTTING COMPLEX(SERINE PROTEASE/COFACTOR/LIGAND), BLOOD COAGULATION, 2 SERINE PROTEASE, COMPLEX, CO-FACTOR, RECEPTOR ENZYME, 3 INHIBITOR, GLA, EGF, COMPLEX (SERINE 4 PROTEASE/COFACTOR/LIGAND), BLOOD CLOTTING	BLOOD CLOTTING COMPLEX(SERINE PROTEASE/COFACTOR/LIGAND), BLOOD COAGULATION, 2 SERINE PROTEASE, COMPLEX, CO-FACTOR, RECEPTOR ENZYME, 3 INHIBITOR, GLA, EGF, COMPLEX (SERINE 4 PROTEASE/COFACTOR/LIGAND), BLOOD CLOTTING	BLOOD CLOTTING COMPLEX(SERINE PROTEASE/COFACTOR/LIGAND), BLOOD COAGULATION, 2 SERINE PROTEASE, COMPLEX, CO-FACTOR, RECEPTOR ENZYME, 3 INHIBITOR, GLA, EGF, COMPLEX (SERINE 4 PROTEASE/COFACTOR/LIGAND), BLOOD CLOTTING	BLOOD CLOTTING COMPLEX(SERINE PROTEASE/COFACTOR/LIGAND), BLOOD COAGULATION, 2 SERINE
Coumpound	CHAIN: I;	BLOOD COAGULATION FACTOR VIIA; CHAIN: L; BLOOD COAGULATION FACTOR VIIA; CHAIN: H; SOLUBLE TISSUB FACTOR; CHAIN: T; 5L15;	BLOOD COAGULATION FACTOR VIIA; CHAIN: L; BLOOD COAGULATION FACTOR VIIA; CHAIN: H; SOLUBLE TISSUB FACTOR; CHAIN: T; 5L15; CHAIN: I;	BLOOD COAGULATION FACTOR VIIA; CHAIN: L; BLOOD COAGULATION FACTOR VIIA; CHAIN: H; SOLUBLE TISSUE FACTOR; CHAIN: T; 5L15; CHAIN: I;	BLOOD COAGULATION FACTOR VIIA; CHAIN: L; BLOOD
SeqFold Score					
PMF Score		0.28	0.23	-0.15	0.07
Verify Score		0.25	-0.10	0.05	-0.28
PSI- BLAST		2.6e-23	2.6e-23	1.3e-08	le-13
End AA		1443	1526	271	379
Start AA		1336	1423	163	286
Chain D		-1	ı	L)	r
PDB CD		1fak	1fak	1fak	1fak
SEQ No.		106	106	106	106

PDB annotation	PROTEASE, COMPLEX, CO-FACTOR, RECEPTOR ENZYME, 3 INHIBITOR, GLA, EGF, COMPLEX (SERINE 4 PROTEASE/COFACTOR/LIGAND), BLOOD CLOTTING	BLOOD CLOTTING COMPLEX(SERINE PROTEASE/COFACTOR/LIGAND), BLOOD COAGULATION, 2 SERINE PROTEASE, COMPLEX, CO-FACTOR, RECEPTOR ENZYME, 3 INHIBITOR, GLA, EGF, COMPLEX (SERINE 4 PROTEASE/COFACTOR/LIGAND), BLOOD CLOTTING	BLOOD CLOTTING COMPLEX(SERINE PROTEASE/COFACTOR/LIGAND), BLOOD COAGULATION, 2 SERINE PROTEASE, COMPLEX, CO-FACTOR, RECEPTOR ENZYME, 3 INHIBITOR, GLA, EGF, COMPLEX (SERINE 4 PROTEASE/COFACTOR/LIGAND), BLOOD CLOTTING	BLOOD CLOTTING COMPLEX(SERINE PROTEASE/COFACTOR/LIGAND), BLOOD COAGULATION, 2 SERINE PROTEASE, COMPLEX, CO-FACTOR, RECEPTOR ENZYME, 3 INHIBITOR, GLA, EGF, COMPLEX (SERINE 4 PROTEASE/COFACTOR/LIGAND), BLOOD CLOTTING
Coumpound	COAGULATION FACTOR VIIA; CHAIN: H; SOLUBLE TISSUE FACTOR; CHAIN: T; 5L15; CHAIN: I;	BLOOD COAGULATION FACTOR VIIA; CHAIN: L; BLOOD COAGULATION FACTOR VIIA; CHAIN: H; SOLUBLE TISSUE FACTOR; CHAIN: T; 5L15; CHAIN: I;	BLOOD COAGULATION FACTOR VIIA; CHAIN: I.; BLOOD COAGULATION FACTOR VIIA; CHAIN: H; SOLUBLE TISSUB FACTOR; CHAIN: T; 5L15; CHAIN: I;	BLOOD COAGULATION FACTOR VILA; CHAIN: L; BLOOD COAGULATION FACTOR VILA; CHAIN: H; SOLUBLE TISSUE FACTOR; CHAIN: T; 5L15;
SeqFold Score				
PMF Score		66:0	0.55	0.07
Verify Score		0.02	0.09	-0.07
PSI- BLAST		2.6e-22	1.36-20	7.8e-19
End AA		575	957	987
Start AA		481	857	897
Chain ID		1	J	ı
PDB ID		1fak	lfak	1fak
SEQ B G		106	106	106

PDB annotation		BLOOD CLOTTING COMPLEX(SERINE PROTEASE/COFACTOR/LIGAND), BLOOD COAGULATION, 2 SERINE PROTEASE, COMPLEX, CO-FACTOR, PROFED DE BUTYME 3 INSTITOR	ACCEL ON EACH INE., S. LYLLEY OF GLA, EGF, COMPLEX (SERINE 4 PROTEASE/COFACTOR/LIGAND), BLOOD CLOTTING	HYDROLASE GODMT-II; LYS49- PHOSPHOLIPASE A2, SNAKE VENOM, BOTHROPS	GROWTH FACTOR NEU DIFFERENTIATION FACTOR (RAT), ACETYLCHOLINE GROWTH FACTOR	HORMONE RECEPTOR HORMONE RECEPTOR, INSULIN RECEPTOR FAMILY	PHOSPHOLIPASE PHOSPHOLIPASE A2, AGKISTRODON HALYS PALLAS CRYSTAL 2 STRUCTURE	GLYCOPROTEIN GLYCOPROTEIN				
Coumpound	CHAIN: I;	BLOOD COAGULATION FACTOR VIIA; CHAIN: L; BLOOD COAGULATION	CHAIN: H; SOLUBLE TISSUB FACTOR; CHAIN: T; 5L15; CHAIN: I;	PHOSPHOLIPASE A2; CHAIN: A;	HERBGULIN-ALPHA; CHAIN: NULL;	INSULIN-LIKE GROWTH FACTOR RECEPTOR 1; CHAIN: A;	PHOSPHOLIPASE A2; CHAIN: A, B;	LAMININ; CHAIN: NULL;	LAMININ; CHAIN: NULL;	LAMININ; CHAIN: NULL;	LAMININ; CHAIN: NULL;	LAMININ; CHAIN:
SeqFold Score												
PMF Score		0.06		-0.19	-0.05	0.04	-0.20	-0.18	-0.13	0.78	-0.20	-0.18
Verify Score		-0.08		0.21	0.80	-0.17	0.10	90:0	0.01	0.27	0.30	0.12
PSI- BLAST		3.4e-10		1.3e-09	5.2e-10	3.9e-10	1.2e-22	1.3e-13	6.5e-21	2.6e-18	1.7e-08	3.4e-11
End AA		1032		290	201	291	1429	246	1533	327	744	868
Start		941	-	158	157	122	1309	129	1352	163	294	735
Chain ID		L		Y		A	V					
PDB ID		lfak		1god	1hae	ligr	ljia	1klo	1klo	Iklo	1klo	1klo
SEQ B SE		106		106	106	106	106	106	106	106	106	106

				2			
PDB annotation		GLYCOPROTEIN GLYCOPROTEIN	GLYCOPROTEIN GLYCOPROTEIN	COMPLEX (BLOOD COAGULATION/INHIBITOR) CHRISTMAS FACTOR; COMPLEX, INHIBITOR, HEMOPHILIA/EGF, BLOOD COAGULATION, 2 PLASMA, SERINB PROTEASE, CALCIUM- BINDING, HYDROLASE, 3 GLYCOPROTEIN	COMPLEX (BLOOD COAGULATION/INHIBITOR) CHRISTMAS FACTOR; COMPLEX, INHIBITOR, HEMOPHILIA/EGF, BLOOD COAGULATION, 2 PLASMA, SERINB PROTEASE, CALCIUM- BINDING, HYDROLASE, 3 GLYCOPROTEIN	COMPLEX (BLOOD COAGULATION/INHIBITOR) CHRISTMAS FACTOR; COMPLEX, INHIBITOR, HEMOPHILIA/EGF, BLOOD COAGULATION, 2 PLASMA, SERINE PROTEASE, CALCIUM- BINDING, HYDROLASE, 3 GLYCOPROTEIN	COMPLEX (BLOOD COAGULATION/INHIBITOR) CHRISTMAS FACTOR; COMPLEX, INHIBITOR, HEMOPHILIA/EGF, BLOOD COAGULATION, 2 PLASMA,
Coumpound	NULL;	LAMININ; CHAIN: NULL;	LAMININ; CHAIN: NULL;	FACTOR IXA; CHAIN: C, L,; D-PHB- PRO-ARG; CHAIN: I;	FACTOR IXA; CHAIN: C, L.; D-PHE- PRO-ARG; CHAIN: I;	FACTOR IXA; CHAIN: C, L.; D-PHB- PRO-ARG; CHAIN: I;	FACTOR IXA; CHAIN: C, L.; D-PHE- PRO-ARG; CHAIN: I;
SeqFold Score							
PMF Score		0.05	0.03	-0.03	0:30	-0.15	0.03
Verify Score		0.14	-0.03	0.08	-0.05	0.17	-0.02
PSI- BLAST		5.2e-14	2.6e-12	2.6e-18	1.3e-22	3.9e-16	2.6e-32
End		930	1027	1229	1408	249	1491
Start AA		771	898	1084	1296	129	1352
Chain ID				<u> 1</u>	7	1	1
PDB CD		1klo	1klo	1pfx	1pfx	1pfx	1pfx
SEQ No:		106	106	106	106	106	106

РDВ annotation	SERINE PROTEASE, CALCIUM- BINDING, HYDROLASE, 3 GLYCOPROTEIN	COMPLEX (BLOOD COAGULATION/INHIBITOR) CHRISTMAS FACTOR; COMPLEX, INHIBITOR, HEMOPHILIA/EGF, BLOOD COAGULATION, 2 PLASMA, SERINE PROTEASE, CALCIUM- BINDING, HYDROLASE, 3 GLYCOPROTEIN	COMPLEX (BLOOD COAGULATION/INHIBITOR) CHRISTMAS FACTOR; COMPLEX, INHIBITOR, HEMOPHILIA/EGF, BLOOD COAGULATION, 2 PLASMA, SERINE PROTEASE, CALCIUM- BINDING, HYDROLASE, 3 GLYCOPROTEIN	COMPLEX (BLOOD COAGULATION/INHIBITOR) CHRISTMAS FACTOR; COMPLEX, INHIBITOR, HEMOPHILIA/EGF, BLOOD COAGULATION, 2 PLASMA, SERINE PROTEASE, CALCIUM- BINDING, HYDROLASE, 3 GLYCOPROTEIN	COMPLEX (BLOOD COAGULATION/INHIBITOR) CHRISTMAS FACTOR; COMPLEX, INHIBITOR, HEMOPHILIA/EGF, BLOOD COAGULATION, 2 PLASMA, SERINE PROTEASE, CALCIUM- BINDING, HYDROLASE, 3 GLYCOPROTEIN
Coumpound		FACTOR IXA; CHAIN: C, L.; D-PHE- PRO-ARG; CHAIN: I;			
SeqFold Score					
PMF Score		0.16	0.12	-0.18	-0.07
Verify Score		-0.03	-0.03	0.02	0.08
PSI- BLAST		6.5e-30	6.5e-24	2.6e-21	1.5e-11
End AA		1535	1550	312	379
Start AA		1391	1436	159	286
Chain U		٦	L1	ы	L]
PDB TD		1pfx	1pfx	1pfx	1pfx
SEQ D D		106	106	106	106

PDB annotation		COMPLEX (BLOOD COAGULATION/INHIBITOR) CHRISTMAS FACTOR; COMPLEX, INHIBITOR, HEMOPHILIA/EGF, BLOOD COAGULATION, 2 PLASMA, SERINE PROTEASE, CALCIUM- BINDING, HYDROLASE, 3 GLYCOPROTEIN		SERINE PROTEASE FVIIA; BLOOD COAGULATION, SERINE PROTEASE	PLASMINOGEN ACTIVATION
Coumpound	FACTOR IXA; CHAIN: C, L.; D-PHB- PRO-ARG; CHAIN: I;	FACTOR IXA; CHAIN: C, L.; D-PHB- PRO-ARG; CHAIN: I;	HYDROLASE CALCIUM-FREE PHOSPHOLIPASE A=2= (E.C.3.1.1.4) 1PP2 4	COAGULATION FACTOR VIIA (LIGHT CHAIN); CHAIN: L; COAGULATION FACTOR VIIA (HEAVY CHAIN); CHAIN: H; TRIPEPTIDYL INHIBITOR; CHAIN: C;	T-PLASMINOGEN ACTIVATOR F1-G; 1TPG 7 CHAIN:
SeqFold Score					
PMF Score	0.40	-0.03	-0.19	0.65	0.19
Verify Score	-0.44	0.13	0.08	0.18	0.02
PSI- BLAST	2.6e-31	1.2e-24	7.8e-19	8.5e-13	3.9e-10
End	575	286	1387	1550	190
Start AA	455	898	1252	1471	119
Chain ID	ប	1	R	7	
PDB ID	1pfx	1pfx	1pp2	1qfk	ltpg
SEQ NO:	106	106	106	106	106

PDB annotation		PLASMINOGEN ACTIVATION	GLYCOPROTEIN GLYCOPROTEIN, HYDROLASE, SERINE PROTEASE, PLASMA, BLOOD 2 COAGULATION FACTOR	GLYCOPROTEIN GLYCOPROTEIN, HYDROLASE, SERINE PROTEASE, PLASMA, BLOOD 2 COAGULATION FACTOR					
Coumpound	NULL; 1TPG 8	T-PLASMINOGEN ACTIVATOR F1-G; ITPG 7 CHAIN: NULL; ITPG 8	T-PLASMINOGEN ACTIVATOR F1-G; 1TPG 7 CHAIN: NULL; 1TPG 8	T-PLASMINOGEN ACTIVATOR F1-G; 1TPG 7 CHAIN: NULL; 1TPG 8	T-PLASMINOGEN ACTIVATOR F1-G; ITPG 7 CHAIN: NULL; ITPG 8	T-PLASMINOGEN ACTIVATOR F1-G; ITPG 7 CHAIN: NULL; ITPG 8	COAGULATION FACTOR X; CHAIN: NULL;	COAGULATION FACTOR X; CHAIN: NULL;	LECTIN (AGGLUTININ) WHEAT GERM AGGLUTININ (ISOLECTIN 2)
SeqFold Score		,							
PMF Score		-0.18	-0.05	0.40	0.34	-0.13	-0.07	0.17	-0.14
Verify Score		0.28	0.04	09.0	-0.20	0.03	0.14	-0.07	0.05
PSI- BLAST		1e-23	5.2e-20	7.8e-16	3.9e-22	2.6e-19	2.6e-12	6.5e-15	6.8e-13
End		1430	1512	220	570	696	222	984	1250
Start		1320	1405	140	471	879	148	906	1081
Chain ID									4
PDB ID		1tpg	1фд	Тфв	ltpg	1tpg	1whe	lwhe	9wga
SEQ EQ		106	106	106	106	106	106	106	106

PDB annotation			SUGAR BINDING PROTEIN C-TYPE LECTIN, CRD, SP-D, COLECTIN, ALPHA-HELICAL COILED- 2 COIL, LUNG SUFFACTANT, SUGAR BINDING PROTEIN	DINDING I NOTELIN	COLLAGEN BINDING PROTEIN IX- BP: IX-BP: COAGULATION FACTOR	IX-BINDING, HETERODIMER,	VENOM, HABU 2 SNAKE, C-TYPE	LECTIN SUPERFAMILY, COLLAGEN	BINDING PROTEIN		COLLAGEN BINDING PROTEIN IX-	BP; IX-BP; COAGULATION FACTOR	IX-BINDING, HETERODIMER,	VENOM, HABU 2 SNAKE, C-TYPE	LECTIN SUPERFAMILY, COLLAGEN	BINDING PROTEIN		MEMBRANE PROTEIN C-TYPE	LECTIN-LIKE DOMAINS		
Coumpound	9WGA 3	LECTIN (AGGLUTININ) WHEAT GERM AGGLUTININ (ISOLECTIN 2) 9WGA 3	LUNG SURFACTANT PROTEIN D; CHAIN: A, B, C;		COAGULATION FACTOR IX-	BINDING PROTEIN	A; CHAIN: A;	COAGULATION	FACTOR IX-	BINDING PROTEIN B; CHAIN: B;	COAGULATION	FACTOR IX-	BINDING PROTEIN	A; CHAIN: A;	COAGULATION	FACTOR IX-	BINDING PROTEIN B: CHAIN: B:	FLAVOCETIN-A:	ALPHA SUBUNIT;	CHAIN: A;	FLAVOCETIN-A: BETA SUBUNIT;
SeqFold Score					69.74												,			_	
PMF Score		-0.19	-0.19								1.00							0.81			
Verify Score		0.09	0.04								0.40							0.38			
PSI- BLAST		3.4e-11	3.4e-18		8.5e-33						8.5e-33							5.1e-31			
End AA		749	312		178						177							180			
Start AA		586	211		83						32							32			
Chain D		4	¥		∢						V							В			
PDB TD		9wga	1608		1bj3						1bj3				·			1c3a			
SE Se Se Se Se Se Se Se Se Se Se Se Se Se		106	108		108						108							108			

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PDB annotation		SIGNALING PROTEIN HEPATIC LECTIN H1; C-TYPE LECTIN CRD	SIGNALING PROTEIN HEPATIC LECTIN H1; C-TYPE LECTIN CRD	SUGAR BINDING PROTEIN C-TYPE LECTIN, MANNOSE RECEPTOR	SUGAR BINDING PROTEIN C-TYPE LECTIN, MANNOSE RECEPTOR	÷		LECTIN TETRANECTIN, PLASMINOGEN BINDING, KRINGLE 4, ALPHA-HELICAL 2 COILED COIL,
p		PROT t 1;	PROT	IAIN:	IAIN:	ON CTIN AINS, 57) SRLY AM-1)	ON CTTIN AINS, 57) SRLY AM-1)	
Coumpound	В	ASIALOGLYCOPROTEIN RECEPTOR 1; CHAIN: A;	ASIALOGLYCOPROT EIN RECEPTOR 1; CHAIN: A;	MACROPHAGE MANNOSE RECEPTOR; CHAIN: A, B;	MACROPHAGE MANNOSE RECEPTOR; CHAIN: A, B;	CELL ADHESION PROTEIN E. SELECTIN (LECTIN AND EGF DOMAINS, RESIDUES 1 - 157) 1ESL 3 (FORMERLY KNOWN AS ELAM-1) 1ESL 4	CELL ADHESION PROTEIN E- SELECTIN (LECTIN AND EGF DOMAINS, RESIDUES 1 - 157) 1ESL 3 (FORMERLY KNOWN AS ELAM-1) 1ESL 4	NECTIN NULL;
ပိ	CHAIN: B	ASIALOGI EIN RECER CHAIN: A;	ASIALOGI EIN RECEF CHAIN: A;	MACROPH MANNOSE RECEPTOR A, B;	MACROPHAGE MANNOSE RECEPTOR; CH A, B;	CELL ADHE PROTEIN E- SELECTIN (AND EGF DI RESIDUES 1 IESL 3 (FOR KNOWN AS	CELL ADHE PROTEIN B- SELECTIN (AND EGF DI RESIDUES 1 1ESL 3 (FOR KNOWN AS	TETRANECTIN; CHAIN: NULL;
SeqFold Score							62.46	61.20
PMF Score		-0.19	0.57	1.00	0.98	0.93		
Verify Score		0.00	0.30	0.26	0.14	0.71		
PSI- BLAST		6.8e-21	5.1e-29	3.4e-30	6.8e-31	3.4e-27	3.4e-27	3.4e-26
End AA		309	177	177	184	187	214	181
Start AA		211	33	33	31	45	46	15
Chain D		V	A	¥	B			
PDB ID		ldv8	14v8 ·	legg	legg	les!	lesi	1htn
SEQ NO:		108	108	108	108	108	108	108

PDB annotation	C-TYPE LECTIN, CARBOHYDRATE RECOGNITION DOMAIN	COAGULATION FACTOR BINDING IXX-BP COAGULATION FACTOR	BINDING, C-TYPE LECTIN, GLA-	DOMAIN 2 BINDING, C-TYPE CRD MOTIF 1 DOP EXCHANGED DIMER	COAGULATION FACTOR BINDING	IX/X-BP COAGULATION FACTOR	BINDING, C-TYPE LECTIN, GLA-	DOMAIN 2 BINDING, C-TYPE CRD	MOTIF, LOOP EXCHANGED DIMER	COAGULATION FACTOR BINDING	IX/X-BP COAGULATION FACTOR	BINDING, C-TYPE LECTIN, GLA-	DOMAIN 2 BINDING, C-TYPE CRD	MOTIF, LOOP EXCHANGED DIMER	COAGULATION FACTOR BINDING	IX/X-BP COAGULATION FACTOR	BINDING, C-TYPE LECTIN, GLA-	DOMAIN 2 BINDING, C-TYPE CRD	MOTIF, LOOP EXCHANGED DIMER	PANCREATIC STONE INHIBITOR	PANCREATIC STONE INHIBITOR,	LECTIN	PANCREATIC STONE INHIBITOR DANCPEATIC STONE INHIBITOR	LECTIN	METAL BINDING PROTEIN	PANCREATIC STONE PROTEIN, PSP;	PANCKEATIC STONE INHIBITOR,	METAL BINDING PROTEIN PANCREATIC STONE PROTEIN, PSP;
Coumpound		COAGULATION FACTORS IX/X-	BINDING PROTEIN;	CHAIN: A, B, C, D, E, F.	COAGULATION	FACTORS IX/X-	BINDING PROTEIN;	CHAIN: A, B, C, D, E,	Ę,	COAGULATION	FACTORS IX/X-	BINDING PROTEIN;	CHAIN: A, B, C, D, E,	Ę	COAGULATION	FACTORS IX/X-	BINDING PROTEIN;	CHAIN: A, B, C, D, E,	F;	LITHOSTATHINE;	CHAIN: NULL		LITHOSTATHINE;		LITHOSTATHINE;	CHAIN: A;		LITHOSTATHINE; CHAIN: A;
SeqFold Score					63.16										55.73								76.77	•	80.98			
PMF Score		1.00								0.48										06:0								-0.15
Verify Score		0.38								0.29										0.56								0.20
PSI- BLAST		8.5e-31			8.5e-31					3.4e-31					3.4e-31					1e-32			le-32		5.1e-34			5.1e-19
End		177			178					180					180					179			180		180			313
Start AA		32			33	·				32					34					33			33		20			210
Chain ID		¥			A					В					В										A			A
PDB ID		lixx			lixx					lixx					lixx					1Iit			Tit.		1qdd			1qdd
og a ç		108			108					108					108					108			108		108			108

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PDB annotation	PANCREATIC STONE INHIBITOR, LITHOSTATHINE	METAL BINDING PROTEIN PANCREATIC STONE PROTEIN, PSP; PANCREATIC STONE INHIBITOR, LITHOSTATHINE	LECTIN TETRANECTIN, PLASMINOGEN BINDING, KRINGLE 4, C-TYPE LECTIN, 2 CARBOHYDRATE RECOGNITION DOMAIN	ANTIFREEZE PROTEIN RECOMBINANT SEA RAVEN PROTEIN, SOLUTION BACKBONE FOLD, C- 2 TYPE LECTIN, ANTIFREEZE PROTEIN	MATRIX PROTEIN EXTRACELLULAR MATRIX, CALCIUM-BINDING, GLYCOPROTEIN, 2 REPEAT, SIGNAL, MULTIGENE FAMILY, DISEASE MUTATION, 3 EGF-LIKE DOMAIN, HUMAN FIBRILLIN-1 FRAGMENT, MATRIX PROTEIN	BLOOD CLOTTING FACTOR VII, BLOOD COAGULATION, EGF-LIKE DOMAIN, BLOOD 2 CLOTTING	GLYCOPROTEIN GLYCOPROTEIN	GLYCOPROTEIN GLYCOPROTEIN	GLYCOPROTEIN GLYCOPROTEIN
Coumpound		LITHOSTATHINE;. CHAIN: A;	TETRANECTIN; CHAIN: NULL;	SEA RAVEN TYPE II ANTIFREEZE PROTEIN; CHAIN: A;	FIBRILLIN; CHAIN: NULL;	BLOOD COAGULATION FACTOR VII; CHAIN: A;	LAMININ; CHAIN: NULL;	LAMININ; CHAIN: NULL;	LAMININ; CHAIN:
SeqFold Score			68.02	·					76.67
PMF Score		66.0		-0.15	-0.17	6.04	-0.19	0.10	
Verify Score		0.42		0.12	0.09	-0.02	60.0	60.0	
PSI- BLAST		5.1e-34	3.4e-26	3.4e-18	3.4e-14	5.1e-07	3.4e-17	3.9e-10	3.4e-17
End		179	181	309	328	72	374	404	406
Start AA		26	29	210	243	% %	239	247	247
Chain ID		A		¥		A			
PDB ID		1qdd	1tm3	2afp	1emn	lf7e	1klo	1klo	1klo
SEQ ID NO:		108	108	108	109	109	109	109	601

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PDB annotation		SERINE PROTEASE FVIIA; FVIIA; BLOOD COAGULATION, SERINE PROTEASE	MEMBRANE ADHESION SHORT CONSENSUS REPEAT, SUSHI, COMPLEMENT CONTROL PROTEIN, 2 N-GLYCOSYLATION, MULTI- DOMAIN, MEMBRANE ADHESION	BLOOD COAGULATION FACTOR STUART FACTOR; BLOOD COAGULATION FACTOR, SERINE PROTEINASE, EPIDERMAL 2 GROWTH FACTOR LIKE DOMAIN			RECEPTOR RECEPTOR, V ALPHA DOMAIN, SITE-DIRECTED
Coumpound	NULL;	COAGULATION FACTOR VIIA (LIGHT CHAIN); CHAIN: L; COAGULATION FACTOR VIIA (HEAVY CHAIN); CHAIN: H; TRIPEPTIDYL INHIBITOR; CHAIN: C;	HUMAN BETA2- GLYCOPROTEIN I; CHAIN: A;	BLOOD COAGULATION FACTOR XA; CHAIN: L, C;	METALLOTHIONEIN METALLOTHIONEIN ISOFORM II 4MT2 3	LECTIN (AGGLUTININ) WHEAT GERM AGGLUTININ (ISOLECTIN 2) 9WGA 3	T-CELL RECEPTOR ALPHA; CHAIN: A,
SeqFold Score			91.30				52.19
PMF Score		-0.13		-0.17	-0.17	-0.19	
Verify Score		0.07		0.08	0.13	0.00	
PSI- BLAST		8.5e-10 -	1.36-14	1.7e-08	6.8e-09	3.46-18	8.5e-29
End AA		110	470	148	339	232	123
Start		39	146	73	276	64	16
Chain TD		T	¥	T		A	V V
PDB ID		1qfk	1qub	lxka	4mt2	9wga	lac6
SEQ B Sign		109	109	109	109	109	110

PDB annotation	MUTAGENESIS, 2 THREE- DIMENSIONAL STRUCTURE, GLYCOPROTEIN, SIGNAL	IMMUNE SYSTEM BENCE-JONES; IMMUNOGLOBULIN, AMYLOID, IMMUNE SYSTEM	IMMUNOGLOBULIN IMMUNOGLOBULIN, KAPPA LIGHT- CHAIN DIMER HEADER	COMPLEX (ANTIBODY/ANTIGEN) FAB-12; VEGF; COMPLEX (ANTIBODY/ANTIGEN), ANGIOGENIC FACTOR	IMMUNE SYSTEM REIV, STABILIZED IMMUNOGLOBULIN FRAGMENT, BENCE-JONES 2 PROTEIN IMMUNE SYSTEM	IMMUNE SYSTEM FAB-IBP COMPLEX CRYSTAL STRUCTURE 2.7A RESOLUTION BINDING 2 OUTSIDE THE ANTIGEN COMBINING SITE SUPERANTIGEN FAB VH3 3 SPECIFICITY		IMMUNE SYSTEM IMMUNOGLOBULIN FOLD, ANTIBODY, IGM, FV	
Coumpound	В;	BENCE-JONES KAPPA I PROTEIN BRE; CHAIN: A, B, C;	IMMUNOGLOBULIN; CHAIN: A, B;	FAB FRAGMENT; CHAIN: L, H, J, K; VASCULAR ENDOTHELIAL GROWTH FACTOR;	CHAIN: V, W; IG KAPPA CHAIN V-1 REGION REI; CHAIN: A, B;	IGM RF 2A2; CHAIN: A, C, E; IGM RF 2A2; CHAIN: B, D, F; IMMUNOGLOBULIN G BINDING PROTEIN A; CHAIN: G, H;	IMMUNOGLOBULIN 3D6 FAB 1DFB 3	IGM MEZ IMMUNOGLOBULIN; CHAIN: L; IGM MEZ IMMUNÒGLOBULIN; CHAIN: H;	IMMUNOGLOBULIN FV FRAGMENT OF A
SeqFold Score		51.99			50.58				52.50
PMF Score			0.62	0.83		0.82	0.83	0.88	
Verify Score			0.49	0.33		0.74	.0.65	0.64	
PSI- BLAST		1.7e-34	3.4e-36	5.1e-38	8.5e-35	5.1e-39	5.1e-36	3.4e-38	8.5e-37
End		123	122	122	122	122	122	122	122
Start AA		14	16	16	13	16	16	16	14
Chain ID		V	A	L)	A	∀	1	ы	L
PDB ID		150w	156d	1bj1	1bw w	1dee	1dfb	1dql	1fgv
S B B S B S		110	110	110	110	110	110	110	110

PDB annotation					COMPLEX (IMMUNOGLOBULIN/RECEPTOR) TCR VAPLHA VBETA DOMAIN; T- CELL RECEPTOR, STRAND SWITCH, FAB, ANTICLONOTYPIC, 2 (IMMUNOGLOBULIN/RECEPTOR)	COMPLEX (IMMUNOGLOBULIN/RECEPTOR) TCR VAPLHA VBETA DOMAIN; T- CELL RECEPTOR, STRAND SWITCH, FAB, ANTICLONOTYPIC, 2
Coumpound	HUMANIZED VERSION OF THE ANTI-CD18 IFGV 3 ANTIBODY 'H52' (HUH52-AA.FV)	IMMUNOGLOBULIN FV FRAGMENT OF A HUMANIZED VERSION OF THE ANTI-CD18 1FGV 3 ANTIBODY 'H52' (HUH52-AA FV) 1FGV 4	IMMUNOGLOBULIN FV FRAGMENT OF HUMANIZED ANTIBODY 4D5, VERSION 8 1FVC 3	IMMUNOGLOBULIN FAB FRAGMENT OF HUMANIZED ANTIBODY 4D5, VERSION 4 1FVD 3	KB5-C20 T-CELL ANTIGEN RECEPTOR; CHAIN: A, B; ANTIBODY DESIRE-1; CHAIN: L,	KB5-C20 T-CELL ANTIGEN RECEPTOR; CHAIN: A, B; ANTIBODY DESIRE-1; CHAIN: L,
SeqFold Score						55.34
PMF Score		0.63	0.77	0.64	0.84	
Verify Score		. 0.30	0.11	0.20	0.46	
PSI- BLAST		8.5e-37	8.5e-37	3.4e-37	1.7e-38	1.7e-38
End AA		122	122	122	123	123
Start AA		16	16	16	15	17
Chain ID		L)	¥	Ą	∢	∢
PDB ID		1fgv	1fvc	lfvd	1kb5	1kb5
SEQ NO:		110	110	110	110	110

PDB annotation	(IMMUNOGLOBULIN/RECEPTOR)	COMPLEX (HYDROLASE/IMMUNOGLOBULIN)		RECEPTOR RECEPTOR, V ALPHA DOMAIN, SITE-DIRECTED MUTAGENESIS, 2 THREE- DIMENSIONAL STRUCTURE, GLYCOPROTEIN, SIGNAL	IMMUNE SYSTEM BENCE-JONES; IMMUNOGLOBULIN, AMYLOID, IMMUNE SYSTEM	IMMUNOGLOBULIN IMMUNOGLOBULIN, KAPPA LIGHT- CHAIN DIMER HEADER	T CELL RECEPTOR TCR; T CELL RECEPTOR, MHC CLASS I, HUMAN IMMUNODEFICIENCY VIRUS, 2 MOLECULAR RECOGNITION	COMPLEX (ANTIBODY/ANTIGEN) FAB-12; VEGF; COMPLEX (ANTIBODY/ANTIGEN),
Coumpound	H;	N9 NEURAMINIDASE; INMB 4 CHAIN: N; INMB 5 FAB NC10; INMB 9 CHAIN: L, H; INMB 10	IMMUNOGLOBULIN FAB FRAGMENT OF A HUMANIZED VERSION OF THE ANTI-CD18 2FGW 3 ANTIBODY 'H52' (HUH52-OZ FAB) 2FGW 4	T-CELL RECEPTOR ALPHA; CHAIN: A, B;	BENCE-JONES KAPPA I PROTEIN BRE; CHAIN: A, B, C;	IMMUNOGLOBULIN; CHAIN: A, B;	T CELL RECEPTOR V-ALPHA DOMAIN; CHAIN: A, B;	FAB FRAGMENT; CHAIN: L, H, J, K; VASCULAR
SeqFold Score		51.23		50.92	51.25		50.11	
PMF Score			0.92			86.0		1.00
Verify Score	•		0.32			09:0		0.37
PSI- BLAST		1.4e-30	5.1e-37	1e-26	3.4e-35	1.7e-37	5.1e-36	3.4e-39
End AA		123	122	120	120	119	120	119
Start AA		14	16	41	=	12	13	12
Chain D		1	ı	¥	¥	¥	¥	ı,
PDB ID		lnmb	2fgw	lacó	150w	1b6d	1588	1bj1
SE Se Se Se		110	110	111	111	111	111	111

PDB annotation	ANGIOGENIC FACTOR	IMMUNE SYSTEM REIV, STABILIZED IMMUNOGLOBULIN FRAGMENT, BENCE-JONES 2 PROTEIN, IMMUNE SYSTEM	IMMUNE SYSTEM FAB-IBP COMPLEX CRYSTAL STRUCTURE 2.7A RESOLUTION BINDING 2 OUTSIDE THE ANTIGEN COMBINING SITE SUPERANTIGEN FAB VH3 3 SPECIFICITY		IMMUNE SYSTEM IMMUNOGLOBULIN FOLD, ANTIBODY, IGM, FV		
Coumpound	ENDOTHELIAL GROWTH FACTOR; CHAIN: V, W;	IG KAPPA CHAIN V-I REGION REI; CHAIN: A, B;	IGM RF 2A2; CHAIN: A, C, E; IGM RF 2A2; CHAIN: B, D, F; IMMUNOGLOBULIN G BINDING PROTEIN A; CHAIN: G, H;	IMMUNOGLOBULIN 3D6 FAB 1DFB 3	IGM MEZ IMMUNOGLOBULIN; CHAIN: L; IGM MEZ IMMUNOGLOBULIN; CHAIN: H;	IMMUNOGLOBULIN FV FRAGMENT OF A HUMANIZED VERSION OF THE ANTI-CD18 1FGV 3 ANTIBODY 'H52' (HUH52-AA FV) 1FGV 4	IMMUNOGLOBULIN FV FRAGMENT OF A HUMANIZED VERSION OF THE ANTI-CD18 1FGV 3 ANTIBODY 'H52'
SeqFold Score		52.25				51.87	
PMF Score			0.96	0.77	0.98	·	96:0
Verify Score			0.72	0.42	0.53		0.77
PSI- BLAST		1e-36	1.7e-40	3.4e-37	1.2e-39	6.8e-38	6.8e-38
End		119	119	119	119	119	119
Start AA		6	12	12	12	11	12
Chain ID		Ą	V	L)	Ţ		ı
PDB CI		lbw w	1dee	qjp1	[dd]	1fgv	1fgv
S B S		1111	111	111	111	111	111

PDB annotation				COMPLEX (IMMUNOGLOBULIN/RECEPTOR) TCR VAPLHA VBETA DOMAIN; T- CELL RECEPTOR, STRAND SWITCH, FAB, ANTICLONOTYPIC, 2 (IMMUNOGLOBULIN/RECEPTOR)	COMPLEX (IMMUNOGLOBULIN/RECEPTOR) TCR VAPLHA VBETA DOMAIN; T- CELL RECEPTOR, STRAND SWITCH, FAB, ANTICLONOTYPIC, 2 (IMMUNOGLOBULIN/RECEPTOR)	COMPLEX (HYDROLASE/IMMUNOGLOBULIN)	
Coumpound	(HUHS2-AA FV) 1FGV 4	IMMUNOGLOBULIN FV FRAGMENT OF HUMANIZED ANTIBODY 4D5, VERSION 8 1FVC 3	IMMUNOGLOBULIN FAB FRAGMENT OF HUMANIZED ANTIBODY 4D5, VERSION 4 1FVD 3	KB5-C20 T-CELL ANTIGEN RECEPTOR; CHAIN: A, B; ANTIBODY DESIRE-1; CHAIN: L,	KB5-C20 T-CELL ANȚIGEN RECEPTOR; CHAIN: A, B; ANTIBODY DESIRE-1; CHAIN: L,	N9 NEURAMINIDASE; INMB 4 CHAIN: N; INMB 5 FAB NC10; INMB 9 CHAIN: L, H; INMB 10	IMMUNOGLOBULIN FAB FRAGMENT OF A HUMANIZED VERSION OF THE
SeqFold Score					54.13	50.60	
PMF Score		0.74	0.39	06:0			0.94
Verify Score		0.29	0.23	0.51			0.35
PSI- BLAST		1.2e-37	3.4e-38	1.7e-38	1.7e-38	5.1e-32	3.4e-38
End AA		119	119	120	120	120	119
Start AA		12	12	13	14	11	12
Chain ID		¥	A	¥	4	H	Ţ
PDB ID		1fvc	1fvd	1kb5	1kb5	1nmb	2fgw
S B S		111	111	11	E	111	111

PDB annotation		CHAPERONE HOP, TPR-DOMAIN, PEPTIDE-COMPLEX, HELICAL REPEAT, HSP90, 2 PROTEIN	CHANGE HOP TOWARM	PEPTIDE-COMPLEX HELICAL	REPEAT, HSP90, 2 PROTEIN BINDING	CHAPERONE HOP, TPR-DOMAIN,	PEPTIDE-COMPLEX, HELICAL	REPEAT, HSC70, 2 HSP70, PROTEIN	CHAPERONE HOP TPR-DOMAIN	PEPTIDE-COMPLEX, HELICAL	REPEAT, HSC70, 2 HSP70, PROTEIN	BINDING	SIGNALING PROTEIN	PEROXISMORE RECEPTOR 1, PTS1-	Br, renovin-5, r151 rro1511	TETRATRICOPEPTIDE REPEAT, TPR.	2 HELICAL REPEAT		SIGNALING PROTEIN	PEROXISMORE RECEPTOR 1, PTS1-	BP, PEROXIN-5, PTS1 PROTEIN-	PEPTIDE COMPLEX,	2 HELICAL REPEAT
Coumpound	ANTJ-CD18 2FGW 3 ANTIBODY 'H52' (HUH52-OZ FAB) 2FGW 4	TPR2A-DOMAIN OF HOP; CHAIN: A; HSP90-PEPTIDE	TED A DOMAIN OF	HOP: CHAIN: A:	HSP90-PEPTIDE MEEVD; CHAIN: B;	TPR1-DOMAIN OF	HOP; CHAIN: A, B;	HSC70-PEPTIDE;	TPR1-DOMAIN OF	HOP: CHAIN: A, B;	HSC70-PEPTIDE;	CHAIN: C, D;	PEROXISOMAL	TARGETING SIGNAL	CHAIN: A B. PTS1.	CONTAINING	PEPTIDE; CHAIN: C,	Ď,	PEROXISOMAL	TARGETING SIGNAL	I RECEPTOR;	CHAIN: A, B; PTS1-	PEPTIDE; CHAIN: C,
SeqFold Score																	•			•	•		
PMF Score		0.27	0 27	7:5		0.40	•	-	0.40	 -			0.28		-				0.28				
Verify Score		-0.21	0.21	17:0-		-0.23			-0.23				-0.40						-0.40				
PSI- BLAST		0.00026	90000	0.0000		0.0052			0.0052		,		0.00013						0.00013				
End		442	277	7		440			440	· ,			45						445	•			-
Start AA		371	271	T/C		374			374				131						131				
Chain		¥	\ <	ς		A			A				V						Ą				
PDB CI		lelr	19			lelw			lelw				1fch						1 fch				
SEQ BO		114	-1.	<u> </u>		114			114			-	114						114				

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PDB annotation		SIGNALING PROTEIN PEROXISMORE RECEPTOR 1, PTS1- BP, PEROXIN-5, PTS1 PROTEIN- PEPTIDE COMPLEX, TETRATRICOPEPTIDE REPEAT, TPR, 2 HELICAL REPEAT	SIGNALING PROTEIN PEROXISMORE RECEPTOR 1, PTS1- BP, PEROXIN-5, PTS1 PROTEIN- PEPTIDE COMPLEX, TETRATRICOPEPTIDE REPEAT, TPR, 2 HELICAL REPEAT		ANTI-ONCOGENE CELL CYCLE, ANTI-ONCOGENE, REPEAT, ANK REPEAT	COMPLEX (TRANSCRIPTION REGULATION/DNA) GABPALPHA; GABPBETA1; COMPLEX (TRANSCRIPTION REGULATION/DNA), DNA-BINDING, 2 NUCLEAR PROTEIN, ETS DOMAIN, ANKYRIN REPEATS, TRANSCRIPTION 3 FACTOR	COMPLEX (TRANSCRIPTION REGULATION/DNA) GABPALPHA; GABPBETA1; COMPLEX (TRANSCRIPTION REGULATION/DNA), DNA-BINDING, 2 NUCLEAR PROTEIN, ETS DOMAIN,
Coumpound	D;	PEROXISOMAL TARGETING SIGNAL I RECEPTOR; CHAIN: A, B; PTSI- CONTAINING PEPTIDE; CHAIN: C,	PEROXISOMAL TARGETING SIGNAL 1 RECEPTOR; CHAIN: A, B; PTS1- CONTAINING PEPTIDE; CHAIN: C, D;		TUMOR SUPPRESSOR P16INK4A; CHAIN: NULL;	GA BINDING PROTEIN ALPHA; CHAIN: A; GA BINDING PROTEIN BETA 1; CHAIN: B; DNA; CHAIN: D, E;	GA BINDING PROTEIN ALPHA; CHAIN: A; GA BINDING PROTEIN BETA 1; CHAIN: B; DNA; CHAIN: D, E;
SeqFold Score							
PMF Score		0.57	0.57		-0.05	1.00	1.00
Verify Score		-0.34	-0.34		0.04	0.93	0.57
PSI- BLAST		9.1e-09	9.1e-09		5.1e-14	1.2e-31	1e-40
End AA		518	518		147	315	349
Start AA		275	275		9	166	195
Chain D		A	∢			æ	æ
PDB ID		1fch	1fch		la5e	lawc	lawc
SEQ B G S		114	114		115	115	115

РДВ вппотатоп	ANKYRIN REPEATS, TRANSCRIPTION 3 FACTOR	COMPLEX (TRANSCRIPTION REGULATION/DNA) GABPALPHA; GABPBETA1; COMPLEX	(TRANSCRIPTION REGULATION/DNA), DNA-BINDING, 2 NUCLEAR PROTEIN, ETS DOMAIN, ANKYRIN REPEATS.	TRANSCRIPTION 3 FACTOR	COMPLEX (TRANSCRIPTION	KEGULATION/DNA) GABPALPHA; GABPBETA1: COMPLEX	(TRANSCRIPTION	REGULATION/DNA), DNA-BINDING,	2 NUCLEAR PROTEIN, ETS DOMAIN, ANKYRIN REPEATS	TRANSCRIPTION 3 FACTOR	COMPLEX (TRANSCRIPTION	REGULATION/DNA) GABPALPHA;	GABPBETA1; COMPLEX	(TRANSCRIPTION PROTIT ATTOMONA) DNA BRIDAG	2 NICLEAR PROTEIN ETS DOMAIN	ANKYRIN REPEATS.	TRANSCRIPTION 3 FACTOR	COMPLEX (TRANSCRIPTION	REGULATION/DNA) GABPALPHA;	GABPBETA1; COMPLEX	(TRANSCRIPTION	REGULATION/DNA), DNA-BINDING,	2 NUCLEAR PROTEIN, ETS DOMAIN,	ANKYKIN KEPEAIS, TRANSCRIPTION 3 FACTOR	TUMOR SUPPRESSOR TUMOR
Coumpound		GA BINDING PROTEIN ALPHA; CHAIN: A; GA	BINDING PROTEIN BETA 1; CHAIN: B; DNA; CHAIN: D, B;		GA BINDING	CHAIN: A: GA	BINDING PROTEIN	BETA 1; CHAIN: B;	DNA; CHAIN: D, E;		GA BINDING	PROTEIN ALPHA;	CHAIN: A; GA	BETA 1: CHAIN: B:	DNA CHAIN D E	(~ (~		GA BINDING	PROTEIN ALPHA;	CHAIN: A; GA	BINDING PROTEIN	BETA 1; CHAIN: B;	DNA; CHAIN: D, E;		P19INK4D CDK4/6
SeqFold Score																									
PMF		-0.06			96.0						1.00							0.71					-		0.47
Verify Score		-0.00			0.29						0.30							0.08							0.22
PSI- BLAST		1.4e-36			3.4e-28	·					1.3e-35							5.1e-28							3.4e-29
End AA		420			215						549				;			181						-	386
Start AA		768			40						69							9							237
Chain ID		В			В	-					В							æ							
PDB ID		lawc			lawc						lawc							1awc					•		1bd8
SEQ ID NO:		1115			115						115							115							115

PDB annotation	SUPPRESSOR, CDK4/6 INHIBITOR, ANKYRIN MOTIF	TUMOR SUPPRESSOR TUMOR SUPPRESSOR, CDK4/6 INHIBITOR, ANKYRIN MOTIF	COMPLEX (KINASE/ANTI- ONCOGENE) CDK6, PI6INK4A, MTS1, CYCLIN DEPENDENT KINASE, CYCLIN DEPENDENT KINASE INHIBITORY 2 PROTEIN, CDK, INK4, CELL CYCLE, MULTIPLE	COMPLEX (KINASE/ANTI- ONCOGENE) HEADER	COMPLEX (INHIBITOR PROTEIN/KINASE) INHIBITOR PROTEIN, CYCLIN-DEPENDENT KINASE, CELL CYCLE 2 CONTROL, ALPHA/BETA, COMPLEX (INHIBITOR PROTEIN/KINASE)	COMPLEX (INHIBITOR PROTEIN/KINASE) INHIBITOR PROTEIN, CYCLIN-DEPENDENT KINASE, CELL CYCLE 2 CONTROL, ALPHA/BETA, COMPLEX (INHIBITOR PROTEIN/KINASE)	COMPLEX (INHIBITOR PROTEIN/KINASE) INHIBITOR PROTEIN, CYCLIN-DEPENDENT KINASE, CELL CYCLE 2 CONTROL, ALPHA/BETA, COMPLEX (INHIBITOR PROTEIN/KINASE)	COMPLEX (INHIBITOR PROTEIN/KINASE) INHIBITOR
Coumpound	INHIBITOR; CHAIN: S NULL; A	P19INK4D CDK4/6 T INHIBITOR; CHAIN: S NULL;	4- DENT 8 6; CHAIN: A; PLE TUMOR SSSOR; B;		ENT 5; CHAIN: A; 2; CHAIN:	CYCLIN- DEPENDENT P KINASE 6; CHAIN: A; P P P19INK4D; CHAIN: K K B; CHAIN: CHAIN: K K B; P CHAIN: CHAIN: K K B; CHAIN: CHAIN: K K B; CHAIN: CHAIN: K K B; CHAIN: K K CHAIN: K C	CYCLIN- DEPENDENT P KINASE 6; CHAIN: A; P P P19INK4D; CHAIN: K B;	CYCLIN- C
SeqFold Score								
PMF Score		0.03	0.05		1.00	1.00	1.00	1.00
Verify Score		0.10	-0.20		0.81	0.44	0.73	0.44
PSI- BLAST		1e-26	3.4e-14		5.2e-40	7.8e-39	5.2e-36	5.2e-27
End		181	147		287	320	348	184
Start AA		6	9		132	166		4
Chain			æ		В	В	В	В
808 CI		1bd8	15:7		1blx	1blx	161x	1bfx
ğa ş		115	115		115	115	115	115

PDB annotation	PROTEIN, CYCLIN-DEPENDENT KINASE, CELL CYCLE 2 CONTROL, ALPHA/BETA, COMPLEX (INHIBITOR PROTEIN/KINASE)	COMPLEX (INHIBITOR PROTEIN/KINASE) INHIBITOR PROTEIN, CYCLIN-DEPENDENT KINASE, CELL CYCLE 2 CONTROL, ALPHA/BETA, COMPLEX (INHIBITOR PROTEIN/KINASE)	HORMONE/GROWTH FACTOR P18- INK4C; CELL CYCLE INHIBITOR, P18INK4C, TUMOR, SUPPRESSOR, CYCLIN- 2 DEPENDENT KINASE, HORMONE/GROWTH FACTOR	HORMONE/GROWTH FACTOR P18- INK4C; CELL CYCLE INHIBITOR, P18INK4C, TUMOR, SUPPRESSOR, CYCLIN- 2 DEPENDENT KINASE, HORMONE/GROWTH FACTOR	SIGNALING PROTEIN HELIX-TURN- HELIX, ANKYRIN REPEAT	SIGNALING PROTEIN HELIX-TURN- HELIX, ANKYRIN REPEAT	SIGNALING PROTEIN HELIX-TURN- HELIX, ANKYRIN REPEAT
Coumpound	KINASE 6; CHAIN: A; P19INK4D; CHAIN: B;	CYCLIN- DEPENDENT KINASE 6; CHAIN: A; P19INK4D; CHAIN: B;	CYCLIN- DEPENDENT KINASE 6 INHIBITOR; CHAIN: A:	CYCLIN- DEPENDENT KINASE 6 INHIBITOR; CHAIN: A:	CYCLIN- DEPENDENT KINASE 4 INHIBITOR B; CHAIN: A;	CYCLIN- DEPENDENT KINASE 4 INHIBITOR B; CHAIN: A;	CYCLIN- DEPENDENT KINASE 4 INHIBITOR B;
SeqFold Score							
PMF Score		1.00	0.28	0.59	0.99	-0.02	0.43
Verify Score		0.59	0.37	0.12	0.37	0.08	0.44
PSI- BLAST		1.3e-36	6.8e-31	1.7e-29	3.9e-29	3,46-14	1.3e-18
End		251	392	186	252	147	151
Start AA		72	234	9	124	9	6
Chain ID		В	¥	٧	¥	¥	¥.
PDB ID	·	1 <u>6</u> 1x	1bu9	1bu9	1d9s	1d9s	1d9s
SEQ NO:		115	115	115	115	115	115

PDB annotation		ENDOCYTOSIS/EXOCYTOSIS SYNAPTOTAGMIN ASSOCIATED 35 KDA PROTEIN, P35A, THREE HELIX BUNDLE	ENDOCYTOSIS/EXOCYTOSIS SYNAPTOTAGMIN ASSOCIATED 35 KDA PROTEIN, P35A, THREE HELIX BUNDLE	CELL CYCLE INHIBITOR P18- INK4C(INK6); CELL CYCLE INHIBITOR, P18-INK4C(INK6), ANKYRIN REPEAT, 2 CDK 4/6 INHIBITOR	CELL CYCLE INHIBITOR P18- INK4C(INK6); CELL CYCLE INHIBITOR, P18-INK4C(INK6), ANKYRIN REPEAT, 2 CDK 4/6 INHIBITOR	CELL CYCLE INHIBITOR P18- INK4C(INK6); CELL CYCLE INHIBITOR, P18-INK4C(INK6), ANKYRIN REPEAT, 2 CDK 4/6 INHIBITOR	TRANSCRIPTION FACTOR P65; P50D; TRANSCRIPTION FACTOR, IKB/NFKB COMPLEX	TRANSCRIPTION FACTOR P65; P50D; TRANSCRIPTION FACTOR, IKB/NFKB COMPLEX
Coumpound	CHAIN: A;	SYNTAXIN-1A; CHAIN: A, B, C;	SYNTAXIN-1A; CHAIN: A, B, C;	CYCLN- DEPENDENT KINASE 6 INHIBITOR; CHAIN: A, B;	CYCLN- DEPENDENT KINASE 6 INHIBITOR; CHAIN: A, B;	CYCLIN- DEPENDENT KINASE 6 INHIBITOR; CHAIN: A, B;	NF-KAPPA-B P65 SUBUNIT; CHAIN: A; NF-KAPPA-B P50D SUBUNIT; CHAIN: C; I-KAPPA-B-ALPHA; CHAIN: D;	NF-KAPPA-B P65 SUBUNIT; CHAIN: A; NF-KAPPA-B P50D SUBUNIT; CHAIN: C;
SeqFold Score								
PMF Score		-0.19	-0.05	0.87	0.77	1.00	66:0	0.24
Verify Score		0.14	0.38	0.24	0.03	0.23	0.41	-0.15
PSI- BLAST		3.9e-08	1.3e-08	3.4e-30	1e-28	1.7e-28	3.4e-38	1.7e-28
End		880	088	391	185	215	348	202
Start		804	817	234	9	08	161	2
Chain ID		¥	¥	V	V	V	Q	D
PDB ID		lez3	lez3	lihb	lihb	1979	likn	likn
S a S		115	115	115	115	115	115	115

PDB annotation		TRANSCRIPTION FACTOR P65; P50D; TRANSCRIPTION FACTOR.	IKB/NFKB COMPLEX			ANK-REPEAT MYOTROPHIN,	COMPLEX (TRANSCRIPTION	REG/ANK REPEAT) COMPLEX	(TRANSCRIPTION	REGULATION/ANK REPEAT),	ANKYRIN 2 REPEAT HELIX		COMPLEX (TRANSCRIPTION	REG/ANK REPEAT) COMPLEX	TOTAL ATTOMINATION	ANEVER 1 DEPENDENT IN THE	ANNIMIN Z KEFEAT HELLA	COMPLEX (TRANSCRIPTION	REG/ANK REPEAT) COMPLEX	(IKAINSCKIPTION	KEGULATION/ANK REPEAT),	ANKYRIN 2 REPEAT HELIX		COMPLEX (TRANSCRIPTION	REG/ANK REPEAT) COMPLEX	(TRANSCRIPTION	REGULATION/ANK REPEAT),	ANKYRIN 2 REPEAT HELIX
Coumpound	I-KAPPA-B-ALPHA; CHAIN: D;	NF-KAPPA-B P65 SUBUNIT; CHAIN: A;	NF-KAPPA-B P50D	SUBUNIT; CHAIN: C; I-KAPPA-B-AI PHA	CHAIN: D;	MYOTROPHIN; CHAIN: NIII I	NF-KAPPA-R P65.	CHAIN: A, C; NF-	KAPPA-B P50;	CHAIN: B, D; I-	KAPPA-B-ALPHA;	CITAIN: E, F;	NF-KAPPA-B P65;	CHAIN: A, C; NF- KAPPA-B PSO-	CUANIC D. 1	KADDA B. AT DHA:	CHAIN: E, F;	NF-KAPPA-B P65;	CHAIN: A, C; NF-	CHAPTER DO	CHAIN: B, D; I-	KAPPA-B-ALPHA;	CHAIN: B, F;	NF-KAPPA-B P65;	CHAIN: A, C; NF-	KAPPA-B P3U;	CHAIN: B, D; I-	KAFFA-B-ALFHA; CHAIN: E, F;
SeqFold Score																									-	-	-	
PMF Score		0.70				99.0	1.00					5	3.1					-0.14						0.98				
Verify Score		0.04				0.07	29.0					0 70	0.48					0.07						0.17				
PSI- BLAST		8.5e-35				le-11	3.4e-38					130.47	1.36-4/		•			3.4e-37						3.4e-35				
End AA		233				26	348					35.4	504					453						233				
Start AA		35				7	159					150	λC1					261						34				
Chain 19		A					E					[n	1					ш					,	1 1				
EQA CE		1ika				1myo	lnfi					1,4	1111	•				lufi Infi						Tur				
SEQ No de		115				115	115					115	CIT					115					ŀ	<u> </u>				

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PDB annotation	COMPLEX (TRANSCRIPTION REG/ANK REPEAT) COMPLEX (TRANSCRIPTION REGULATION/ANK REPEAT), ANKYRIN 2 REPEAT HELIX	COMPLEX (TRANSCRUPTION REG/ANK REPEAT) COMPLEX (TRANSCRIPTION REGULATION/ANK REPEAT), ANKYRIN 2 REPEAT HELIX	COMPLEX (TRANSCRIPTION REG/ANK REPEAT) COMPLEX (TRANSCRIPTION REGULATION/ANK REPEAT), ANKYRIN 2 REPEAT HELIX	COMPLEX (AN11-ONCOGENE/ANKYRIN REPEATS) P53BP2; ANKYRIN REPEATS, SH3, P53, TUMOR SUPPRESSOR, MULTIGENE 2 FAMILY, NUCLEAR PROTEIN, PHOSPHORYLATION, DISEASE MUTATION, 3 POLYMORPHISM, COMPLEX (ANTI-ONCOGENE/ANKYRIN REPEATS)	COMPLEX (TRANSCRIPTION REGULATION/DNA) GABPALPHA; GABPBETA1; COMPLEX (TRANSCRIPTION REGULATION/DNA), DNA-BINDING, 2 NUCLEAR PROTEIN, ETS DOMAIN, ANKYRIN REPEATS,
Coumpound	NF-KAPPA-B P65; CHAIN: A, C; NF- KAPPA-B P50; CHAIN: B, D; I- KAPPA-B-ALPHA; CHAIN: E, F;	NF-KAPPA-B P65; CHAIN: A, C; NF- KAPPA-B P50; CHAIN: B, D; I- KAPPA-B-ALPHA; CHAIN: E, F;	NF-KAPPA-B P65; CHAIN: A, C; NF- KAPPA-B P50; CHAIN: B, D; I- KAPPA-B-ALPHA; CHAIN: E, F;	P53; CHAIN: A; 53BP2; CHAIN: B;	GA BINDING PROTEIN ALPHA; CHAIN: A; GA BINDING PROTEIN BETA 1; CHAIN: B; DNA; CHAIN: D, E;
SeqFold Score					
PMF Score	66.0	0.83	1.00	0.70	1.00
Verify Score	0.41	0.28	0.64	0.39	0.79
PSI- BLAST	3.9e-36	5.1e-27	1.2e-40	3.4e-14	1.7e-34
End	250	165	289	57	315
Start	39	4	69	2	166
Chain	Ш	ш	ш	æ	æ
PDB DD	Infi	1nfi	1nfi	1ycs	lawc
SEQ E	115	115	115	115	116

PDB annotation	FACTOR	SCRIPTION A) GABPALPHA; PLEX	(TRANSCRIPTION REGULATION/DNA), DNA-BINDING,	EIN, ETS DOMAIN,	FACTOR	SCRIPTION	PLEX		REGULATION/DNA), DNA-BINDING,	2 NUCLEAR PROTEIN, ETS DOMAIN,	FACTOR	CRIPTION	A) GABPALPHA;	PLEX		REGULATION/DNA), DNA-BINDING,	2 NUCLEAR PROTEIN, ETS DOMAIN,	is,	TACION.	SCRIPTION 4) GABPALPHA:	PLEX	:	A), DNA-BINDING,	2 NUCLEAR PROTEIN, ETS DOMAIN,	ß,	3 FACTOR	SCRIPTION A) GABPALPHA;
PDB an	TRANSCRIPTION 3 FACTOR	COMPLEX (TRANSCRIPTION REGULATION/DNA) GABPALPHA; GABPBETA1; COMPLEX	(TRANSCRIPTION REGULATION/DN/	2 NUCLEAR PROTEIN, ETS DOMAIN,	TRANSCRIPTION 3 FACTOR	COMPLEX (TRANSCRIPTION	GABPBETA1; COMPLEX	(TRANSCRIPTION	REGULATION/DN.	2 NUCLEAR PROTEIN	TRANSCRIPTION 3 FACTOR	COMPLEX (TRANSCRIPTION	REGULATION/DNA) GABPALPHA;	GABPBETA1; COMPLEX	(TRANSCRIPTION	REGULATION/DN.	2 NUCLEAR PROT	ANKYRIN REPEATS,	I KAINSCALF LIOIN	COMPLEX (TRANSCRIPTION REGII.ATION/DNA) GABPALPHA:	GABPBETA1; COMPLEX	(TRANSCRIPTION	REGULATION/DNA), DNA-BINDING,	2 NUCLEAR PROT	ANKYRIN REPEATS	TRANSCRIPTION 3 FACTOR	COMPLEX (TRANSCRIPTION REGULATION/DNA) GABPALPHA;
Coumpound		GA BINDING PROTEIN ALPHA; CHAIN: A; GA	BINDING PROTEIN BETA 1: CHAIN: B:	DNA; CHAIN: D, E;		GA BINDING	CHAIN: A; GA	BINDING PROTEIN	BETA 1; CHAIN: B;	DNA; CHAIN: D, E;		GA BINDING	PROTEIN ALPHA;	CHAIN: A; GA	BINDING PROTEIN	BETA 1; CHAIN: B;	DNA; CHAIN: D, E;			GA BINDING PROTFIN ALPHA:	CHAIN: A; GA	BINDING PROTEIN	BETA 1; CHAIN: B;	DNA; CHAIN: D, E;			GA BINDING PROTEIN ALPHA;
SeqFold Score																						-					
PMF Score		1.00			•	1.00		·····				1.00								0.29							1.00
Verify Score		0.57				0.73						0.43								0.20							0.30
PSI- BLAST		1e-40				1.7e-36						5.1e-34								1.7e-34							1.3e-35
End		349				348						382								399							249
Start AA		195				200						234								268							69
Chain ID		B				В				-		В								Д							В
PDB ID		lawc				lawc						lawc								lawc							lawc
SEQ El SE		116				116						116								116							116

Coumpound PDB annotation	CHAIN: A; GA BINDING PROTEIN BINDING PROTEIN BETA 1; CHAIN: B; DNA; CHAIN: D, E; ANKYRIN PEPFATS CHAIN: D, E; ANKYRIN PEPFATS	GA BINDING COMPLEX (TRANSCRIPTION PROTEIN ALPHA; CHAIN: A; GA BINDING PROTEIN (TRANSCRIPTION REGULATION/DNA) GABPALPHA; GABPBETA1; COMPLEX BINDING PROTEIN (TRANSCRIPTION REGULATION/DNA), DNA-BINDING, DNA; CHAIN: B; ANKYRIN REPEATS,	GA BINDING COMPLEX (TRANSCRIPTION PROTEIN ALPHA; CHAIN: A; GA BINDING PROTEIN BETA 1; CHAIN: B; CHAIN: B; CHAIN: B; COMPLEX GABPBETA1; COMPLEX GABPBETA1; COMPLEX GABPBETA1; COMPLEX GABPBETA1; COMPLEX GABPBETA1; COMPLEX TRANSCRIPTION DNA; CHAIN: B; ANKYRIN REPEATS, TRANSCRIPTION 3 FACTOR	P19INK4D CDK4/6 TUMOR SUPPRESSOR TUMOR INHIBITOR; CHAIN: SUPPRESSOR, CDK4/6 INHIBITOR, NULL;	4D CDK4/6 FOR; CHAIN:	P19INK4D CDK4/6 TUMOR SUPPRESSOR TUMOR INHIBITOR; CHAIN: SUPPRESSOR, CDK4/6 INHIBITOR, NULL;	t- DENT
SeqFold Score	Δ M M Δ					ZAZ	DO
PMF Score		89.0	66:0	1.00	1.00	0.17	1.00
Verify Score		0.09	0.26	0.28	0.50	0.10	0.57
PSI- BLAST		1.4e-27	1.76-29	1.7e-27	3.4e-31	5.1e-12	le-25
End AA		181	215	249	385	113	249
Start AA		9	76	101	237	2	101
Chain ID		В	m				æ
PDB TD		lawc	lawc	1bd8	1bd8	1bd8	1blx
SEQ No de		116	116	116	116	116	116

PDB annotation	KINASE, CELL CYCLE 2 CONTROL, ALPHA/BETA, COMPLEX (INHIBITOR PROTEIN/KINASE)	COMPLEX (INHIBITOR PROTEIN/KINASE) INHIBITOR PROTEIN, CYCLIN-DEPENDENT KINASE, CELL CYCLE 2 CONTROL, ALPHA/BETA, COMPLEX (INHIBITOR PROTEIN/KINASE)	COMPLEX (INHIBITOR PROTEIN/KINASE) INHIBITOR PROTEIN, CYCLIN-DEPENDENT KINASE, CELL CYCLE 2 CONTROL, ALPHA/BETA, COMPLEX: (INHIBITOR PROTEIN/KINASE)			COMPLEX (INHIBITOR PROTEIN/KINASE) INHIBITOR PROTEIN, CYCLIN-DEPENDENT KINASE, CELL CYCLE 2 CONTROL, ALPHA/BETA, COMPLEX (INHIBITOR PROTEIN/KINASE)	COMPLEX (INHIBITOR
Coumpound	P19INK4D; CHAIN: B;	CYCLIN- DEPENDENT KINASE 6; CHAIN: A; P19INK4D; CHAIN: B;	CYCLN- DEPENDENT KINASE 6; CHAIN: A; P19INK4D; CHAIN: B;	CYCLN- DEPENDENT KINASE 6; CHAIN: A; P19INK4D; CHAIN: B;	CYCLIN- DEPENDENT KINASE 6; CHAIN: A; P19INK4D; CHAIN: B;	CYCLN- DEPBNDENT KINASE 6; CHAIN: A; P19INK4D; CHAIN: B;	CYCLIN-
SeqFold Score							'
PMF		1.00	1.00	1.00	1.00	1.00	1.00
Verify Score		0.81	0.44	0.73	0.56	0.44	0.59
PSI- BLAST		5.2e-40	7.8e-39	5.2e-36	1.4e-31	5.2e-27	1.3e-36
End		287	320	348	385	184	251
· Start AA		132	166	198	237	4	72
Chain ID		m	B	æ	g	æ	В
FDB DD		1blx	1blx	1blx	1blx	1blx	1blx
SEQ B B		116	116	116	116	116	116

PDB annotation	PROTEIN/KINASE) INHIBITOR PROTEIN, CYCLIN-DEPENDENT KINASE, CELL CYCLE 2 CONTROL, ALPHA/BETA, COMPLEX (INHIBITOR PROTEIN/KINASE)	HORMONE/GROWTH FACTOR P18- INK4C; CELL CYCLE INHIBITOR, P18INK4C, TUMOR, SUPPRESSOR, CYCLIN- 2 DEPENDENT KINASE, HORMONE/GROWTH FACTOR	HORMONE/GROWTH FACTOR P18- INK4C; CELL CYCLE INHIBITOR, P18INK4C, TUMOR, SUPPRESSOR, CYCLIN- 2 DEPENDENT KINASE, HORMONE/GROWTH FACTOR	HORMONE/GROWTH FACTOR P18- INK4C; CELL CYCLE INHIBITOR, P18INK4C, TUMOR, SUPPRESSOR, CYCLIN- 2 DEPENDENT KINASE, HORMONE/GROWTH FACTOR	SIGNALING PROTEIN HELIX-TURN- HELIX, ANKYRIN REPEAT	ENDOCYTOSIS/EXOCYTOSIS SYNAPTOTAGMIN ASSOCIATED 35 KDA PROTEIN, P35A, THREE HELLX BUNDLE	ENDOCYTOSIS/EXOCYTOSIS SYNAPTOTAGMIN ASSOCIATED 35 KDA PROTEIN, P35A, THREE HELIX BUNDLE	CELL CYCLE INHIBITOR P18-
Coumpound	DEPENDENT KINASE 6; CHAIN: A; P19INK4D; CHAIN: B;	CYCLIN- DEPENDENT KINASE 6 INHIBITOR; CHAIN: A;	CYCLIN- DEPENDENT KINASE 6 INHIBITOR; CHAIN: A;	CYCLIN- DEPENDENT KINASE 6 INHIBITOR; CHAIN: A;	CYCLIN- DEPENDENT KINASE 4 NHIBITOR B; CHAIN: A;	SYNTAXIN-1A; CHAIN: A, B, C;	SYNTAXIN-1A; CHAIN: A, B, C;	CYCLIN-
SeqFold Score								
PMF Score		1.00	99.0	0.64	0.43	-0.19	-0.05	1.00
Verify Score		0.84	0.29	0.15	0.44	0.14	0.38	0.61
PSI- BLAST		1.5e-30	1.4e-35	5.1e-28	1.3e-18	3.9e-08	1.3e-08	6.8e-30
End AA		288	387	186	151	822	822	287
Start AA		132	234	9	6	746	759	132
Chain TO		A	V	V	«	A	A	A
PDB ID	4:	1bu9	1bu9	1bu9	1d9s	lez3	lez3	1jb
SEQ B B S		116	116	116	116	116	116	116

PDB annotation	INK4C(INK6); CELL CYCLE INHIBITOR, P18-INK4C(INK6), ANKYRIN REPEAT, 2 CDK 4/6 INHIBITOR	CELL CYCLE NHIBITOR P18- INK4C(INK6); CELL CYCLE INHIBITOR, P18-INK4C(INK6), ANKYRIN REPEAT, 2 CDK 4/6 INHIBITOR	CELL CYCLE NHIBITOR P18- NK4C(INK6); CELL CYCLE NHIBITOR, P18-INK4C(INK6), ANKYRIN REPEAT, 2 CDK 4/6 NHIBITOR	TRANSCRIPTION FACTOR P65; P50D; TRANSCRIPTION FACTOR, IKB/NFKB COMPLEX	TRANSCRIPTION FACTOR P65; P50D; TRANSCRIPTION FACTOR, IKB/NFKB COMPLEX	TRANSCRIPTION FACTOR P65; P50D; TRANSCRIPTION FACTOR, IKB/NFKB COMPLEX	TRANSCRIPTION FACTOR P65; P50D; TRANSCRIPTION FACTOR,
Coumpound	DEPENDENT KINASE 6 INHIBITOR; CHAIN: A, B;	CYCLN- DEPENDENT KINASE 6 INHIBITOR; CHAIN: A, B;	CYCLN- DEPENDENT KINASE 6 INHIBITOR; CHAIN: A, B;	NF-KAPPA-B P65 SUBUNIT; CHAIN: A; NF-KAPPA-B P50D SUBUNIT; CHAIN: C; I-KAPPA-B-ALPHA; CHAIN: D;	NF-KAPPA-B P65 SUBUNIT; CHAIN: A; NF-KAPPA-B P50D SUBUNIT; CHAIN: C; I-KAPPA-B-ALPHA; CHAIN: D;	NF-KAPPA-B P65 SUBUNIT; CHAIN: A; NF-KAPPA-B P50D SUBUNIT; CHAIN: C; I-KAPPA-B-ALPHA; CHAIN: D;	NF-KAPPA-B P65 SUBUNIT; CHAIN: A;
SeqFold Score						·	
PMF Score		0.94	0.58	1.00	1.00	0.19	0.22
Verify Score		0.46	0.03	0.35	0.29	0.15	0.05
PSI- BLAST		5.1e-35	1.7e-27	6.8e-34	1.5e-37	1.7e-33	5.1e-28
End		386	185	299	348	399	199
Start AA		234	9	127	161	229	2
Chain		¥	V	Q	Q	Ω	Ω
PDB UD		lihb	11/10	lika	1ika	1ikm	lika
SEQ EQ		116	116	116	116	116	116

PDB annotation	IKB/NFKB COMPLEX	ANK-REPEAT MYOTROPHIN, ACETYLATION, NMR, ANK-REPEAT	COMPLEX (TRANSCRIPTION	REG/ANK REPEAT) COMPLEX	REGULATION/ANK REPEAT),	ANKYRIN 2 REPEAT HELIX	COMPLEX (TRANSCRIPTION	REG/ANK REPEAT) COMPLEX	(TRANSCRIPTION	REGULATION/ANK REPEAT),	ANKYRIN 2 REPEAT HELIX	COMPLEX (TRANSCRIPTION	REG/ANK REPEAT) COMPLEX	(TRANSCRIPTION	REGULATION/ANK REPEAT),	ANKYRIN 2 REPEAT HELIX	COMPLEX (TRANSCRIPTION	REG/ANK REPEAT) COMPLEX	(TRANSCRIPTION	REGULATION/ANK REPEAT),	ANKYRIN 2 REPEAT HELIX		COMPLEX (TRANSCRIPTION REG/ANK REPEAT) COMPLEX	(TRANSCRIPTION	REGULATION/ANK REPEAT),
Coumpound	NF-KAPPA-B P50D SUBUNIT; CHAIN: C; I-KAPPA-B-ALPHA; CHAIN: D;	MYOTROPHIN; CHAIN: NULL	NF-KAPPA-B P65;	CHAIN: A, C; NF- KAPPA-R P50:	CHAIN: B, D; I-	KAPPA-B-ALPHA; CHAIN: E. F.	NF-KAPPA-B P65;	CHAIN: A, C; NF-	KAPPA-B P50;	CHAIN: B, D; I-	KAPPA-B-ALPHA; CHAIN: E, F;	NF-KAPPA-B P65;	CHAIN: A, C; NF-	KAPPA-B P50;	CHAIN: B, D; I-	KAPPA-B-ALPHA; CHAIN: E, F;	NF-KAPPA-B P65;	CHAIN: A, C; NF-	KAPPA-B P50;	CHAIN: B, D; I-	KAPPA-B-ALPHA;	CHAIN: E, F;	NF-KAPPA-B P65; CHAIN: A, C; NF-	KAPPA-B P50;	CHAIN: B, D; I-
SeqFold Score															-										
PMF Score		0.87	1.00				1.00		-			1.00					0.51						-0.14		
Verify Score		-0.09	92.0				0.72			-		0.58					0.38						0.10		
PSI- BLAST		3.4e-12	1.7e-34				7.8e-48					8.5e-38					3.4e-33						1.4e-33		
End AA		.28	565				356					348					399						4		
Start AA		2	125				159					191					877						263	_	
Chain ID			ы				Э	-				B					E						m)	•	
PDB ID		lmyo	lnfi			- :	lnfi					1nfi					1mfi	_				1	Juli Juli		1
SEQ NO B		116	116				116					116					116					,	116		

PDB annotation	ANKYRIN 2 REPEAT HELIX	COMPLEX (TRANSCRIPTION REG/ANK REPEAT) COMPLEX	(IKANSCKIPTION REGULATION/ANK REPEAT), ANKYRIN 2 REPEAT HELIX	COMPLEX (TRANSCRIPTION REG/ANK REPEAT) COMPLEX	(TRANSCRIPTION REGULATION/ANK REPEAT),	ANKYRIN 2 REPEAT HELIX	COMPLEX (TRANSCRIPTION PROJANY PEPRATI COMPLEX	(TRANSCRIPTION	REGULATION/ANK REPEAT),	ANKIKIN Z KEPEAT HELIX	COMPLEX (ANTI- ONCOGENE/ANKYRIN REPEATS) D53BD: ANKVDIN PEBEATS 5H3	P53, TUMOR SUPPRESSOR,	MULTIGENE 2 FAMILY, NUCLEAR PROTEIN, PHOSPHORYLATION.	DISEASE MUTATION, 3	POLYMORPHISM, COMPLEX (ANTI- ONCOGENE/ANKYRIN REPEATS)	ZINC FINGER HOLB; ZINC FINGER, DNA REPLICATION	HEXAMERIZATION DOMAIN
Coumpound	KAPPA-B-ALPHA; CHAIN: E, F;	NF-KAPPA-B P65; CHAIN: A, C; NF-	KAPPA-B P30; CHAIN: B, D; I- KAPPA-B-ALPHA; CHAIN: E, F;	NF-KAPPA-B P65; - CHAIN: A, C; NF-	KAPPA-B P50; CHAIN: B, D; I-	KAPPA-B-ALPHA; CHAIN: E, F;	NF-KAPPA-B P65;	KAPPA-B P50;	CHAIN: B, D; I-	KAPPA-B-ALPHA; CHAIN: E, F;	P53; CHAIN: A; 53BP2; CHAIN: B;					DELTA PRIME; CHAIN: NULL;	N-
SeqFold Score																	
PMF Score		0.19		0.99			1.00				0.70	1				-0.05	0.65
Verify Score		0.28		0.41			0.64				0.39					0.25	0.55
PSI- BLAST		3.4e-28		3.9e-36			1.2e-40				1.2e-13					6.8e-14	3.4e-29
End		199		250			289				57					455	999
Start		2		39			69				2					150	401
Chain ID		Ħ		ш			田				æ						A
PDB CD		Infi		lnfi			Infi				1ycs					laSt	1d2n
SEQ No d		116		116			116				116					117	119

PDB annotation	HEXAMERIZATION DOMAIN, ATPASE, TRANSPORT	CHAPERONE HSLV; HSLU CHAPERONE, HSLVU, CLPQY, AAA- ATPASE, ATP-DEPENDENT 2 PROTEOLYSIS, PROTEASOME	CHAPERONE HSLV; HSLU CHAPERONE, HSLVU, CLPQY, AAA- ATPASE, ATP-DEPENDENT 2 PROTEOLYSIS, PROTEASOME	CHAPERONE AAA-ATPASE, CLPY, ATP-DEPENDENT PROTEOLYSIS	TRANSFERASE SHIKIMATE KINASE, PHOSPHORYL TRANSFER, ADP, SHIKIMATE 2 PATHWAY, P-LOOP PROTEIN, TRANSFERASE		HYDROLASE PROSEGMENT, PROPEPTIDE, INHIBITION, HYDROLASE	HYDROLASE PROSEGMENT, PROPEPTIDE, INHIBITION, HYDROLASE
Coumpound	ETHYLMALEIMIDE- SENSITIVE FUSION PROTEIN; CHAIN: A;	HEAT SHOCK PROTEIN HSLV; CHAIN: A, B, C, D; HEAT SHOCK PROTEIN HSLU; CHAIN: E, F;	HEAT SHOCK PROTEIN HSLV; CHAIN: A, B, C, D; HEAT SHOCK PROTEIN HSLU; CHAIN: E, F;	HEAT SHOCK PROTEIN HSLU; CHAIN: A;	SHIKIMATE KINASE; CHAIN: A, B;	TRANSFERASE(PHO SPHOTRANSFERASE) ADENYLATE KINASE (E.C.2.7.4.3) 3ADK 4	HUMAN PROCATHEPSIN L; CHAN: A;	HUMAN PROCATHEPSIN L; CHAN: A;
SeqFold Score							497.56	497.56
PMF Score		0.21	0.31	0.13	90.0	0.01		
Verify Score		-0.54	-0.30	-0.06	-0.62	0.09		
PSI- BLAST		5.1e-13	3.4e-05	1.7e-18	0.0024	3.9e-05	0	0
End AA		489	577	959	466	599	333	333
Start		388	496	388	437	434	19	19
Chain D		ш	щ	¥	¥		¥.	A
PDB.		1e94	1e94	1841	1shk	3adk	lcs8	lcs8
S B S		119	119	119	119	119	120	120

PDB annotation	HYDROLASE PROSEGMENT, PROPEPTIDE, INHIBITION, HYDROLASE			HYDROLASE II FRAGMENT, CD74 FRAGMENT CYSTEINE PROTEINASE, CATHEPSIN, MHC CLASS II, INVARIANT 2 CHAIN, THYROGLOBULIN TYPE-1 DOMAIN	DE LIPID DEGRADATION PLC-DI; PHOSPHORIC DIESTER C, HYDROLASE, HYDROLASE, LIPID DEGRADATION, 2 TRANSDUCER, CALCIUM-BINDING, PHOSPHOLIPASE C, 3 PHOSPHOLIPASE C, 3	DE LIPID DEGRADATION PLC-D1; PHOSPHORIC DIESTER C, HYDROLASE, HYDROLASE, LIPID DEGRADATION 2 TRANSDUCER.
Coumpound	HUMAN PROCATHEPSIN L; CHAIN: A;	HUMAN PROCATHEPSIN L; CHAIN: A;	CATHEPSIN L: HEAVY CHAIN; CHAIN: A, C; CATHEPSIN L: LIGHT CHAIN; CHAIN: B, D; INVARIANT CHAIN; CHAIN: 1, J;	CATHEPSIN L: HEAVY CHAIN; CHAIN: A, C; CATHEPSIN L: LIGHT CHAIN; CHAIN: B, D; INVARIANT CHAIN; CHAIN: I, J;	PHOSPHOINOSITIDE -SPECIFIC PHOSPHOLIPASE C, CHAIN: A, B;	PHOSPHOINOSITIDE -SPECIFIC PHOSPHOLIPASE C,
SeqFold Score					519.97	519.97
PMF Score	1.00	1.00	0.90	0.90		
Verify Score	0.83	0.83	-0.53	-0.53		
PSI. BLAST	0	0	1.7e-17	1.7e-17	0	0
End	333	333	333	333	793	793
Start	21	21	292	292	242	242
Chafn	A	A	В	æ	A	A
PDB D	1cs8	lcs8	licf	licf	1djx	1djx
SE SE SE SE SE SE SE SE SE SE SE SE SE S	120	120	120	120	121	121

	TC	DI; LIPID JCER,	DI; LIPID JCBR,	DI; LIPID JCER, IC	DI; LIPID JCER, TC	ol; LIPID ICER,
PDB annotation	JING, SEC, 3 TIDE-SPECII	ATION PLC.] UESTER IYDROLASE I, 2 TRANSDI II, 2 TRANSDI ING, IE C, 3	ATION PLC-I IESTER YYDROLASE, ; 2 TRANSDI NING, (E C, 3	ATION PLC-I IESTER YDROLASE, , 2 TRANSDI VING, E C, 3	ATION PLC-I IESTER YDROLASE, , 2 TRANSDI ING, E C, 3	ATION PLC-I IESTER YDROLASE, , 2 TRANSDU
PDB	CALCIUM-BINDING, PHOSPHOLIPASE C, 3 PHOSPHOINOSITIDE-SPECIFIC	LIPID DEGRADATION PLC-D1; PHOSPHORIC DIESTER HYDROLASE, HYDROLASE, LIPID DEGRADATION, 2 TRANSDUCER, CALCIUM-BINDING, PHOSPHOLIPASE C, 3 PHOSPHOINOSITIDE-SPECIFIC	LIPID DEGRADATION PLC-D1; PHOSPHORIC DIESTER HYDROLASE, HYDROLASE, LIPID DEGRADATION, 2 TRANSDUCER, CALCIUM-BINDING, PHOSPHOLIPASE C, 3 PHOSPHOINOSITIDE-SPECIFIC	LIPID DEGRADATION PLC-D1; PHOSPHORIC DIESTER HYDROLASE, HYDROLASE, LIPID DEGRADATION, 2 TRANSDUCER, CALCIUM-BINDING, PHOSPHOLIPASE C, 3 PHOSPHOINOSITIDE-SPECIFIC	LIPID DEGRADATION PLC-D1; PHOSPHORIC DIESTER HYDROLASE, HYDROLASE, LIPID DEGRADATION, 2 TRANSDUCER, CALCIUM-BINDING, PHOSPHOLIPASE C, 3 PHOSPHOINOSITIDE-SPECIFIC	LIPID DEGRADATION PLC-D1; PHOSPHORIC DIESTER HYDROLASE, HYDROLASE, LIPID DEGRADATION, 2 TRANSDUCER,
Coumpound		PHOSPHOINOSITIDE -SPECIFIC PHOSPHOLIPASE C, CHAIN: A, B;	PHOSPHOINOSITIDE -SPECIFIC PHOSPHOLIPASE C, CHAIN: A, B;			
SeqFold Score				571.84	571.84	
PMF Score		1.00	1.00			1.00
Verify Score		0.65	0.68			0.65
PSI- BLAST		0	0	0	0	0
End		792	792	793	793	792
Start AA		259	259	200	200	201
Chain ID		V	¥	B	æ	В
PDB ID		1djx	1djx	1djx	1djx	Idjx
SEQ NO:		121	121	121	121	121

PDB annotation	CALCIUM-BINDING, PHOSPHOLIPASE C, 3 PHOSPHOINOSITIDE-SPECIFIC	LIPID DEGRÁDATION PLC-D1; PHOSPHORIC DIESTER HYDROLASE, HYDROLASE, LIPID DEGRADATION, 2 TRANSDUCER, CALCIUM-BINDING, PHOSPHOLIPASE C, 3 PHOSPHOINOSITIDE-SPECIFIC	METAL TRANSPORT CALMODULIN, HIGH RESOLUTION, DISORDER	METAL TRANSPORT CALMODULIN, HIGH RESOLUTION, DISORDER	SIGNAL TRANSDUCTION PROTEIN PLECKSTRIN, PHOSPHOLIPASE, INOSITOL TRISPHOSPHATE, 2 SIGNAL TRANSDUCTION PROTEIN, HYDROLASE	SIGNAL TRANSDUCTION PROTEIN PLECKSTRIN, PHOSPHOLIPASE, INOSITOL TRISPHOSPHATE, 2 SIGNAL TRANSDUCTION PROTEIN, HYDROLASE	SIGNAL TRANSDUCTION PROTEIN PLECKSTRIN, PHOSPHOLIPASE, INOSITOL TRISPHOSPHATE, 2 SIGNAL TRANSDUCTION PROTEIN, HYDROLASE	SIGNAL TRANSDUCTION PROTEIN PLECKSTRIN, PHOSPHOLIPASE, INOSITOL TRISPHOSPHATE, 2 SIGNAL TRANSDUCTION PROTEIN, HYDROLASE
Coumpound	·	PHOSPHOINOSITIDE -SPECIFIC PHOSPHOLIPASE C, CHAIN: A, B;	CALMODULIN; CHAIN: A;	CALMODULIN; CHAIN: A;	PHOSPHOLIPASE C DELTA-1; CHAIN: NULL;	PHOSPHOLIPASE C DELTA-1; CHAIN: NULL;	PHOSPHOLIPASE C DELTA-1; CHAIN: NULL;	PHOSPHOLIPASE C DELTA-1; CHAIN: NULL;
SeqFold Score			•				110.09	110.09
PMF Score		1.00	0.07	20.0	1.00	1.00		
Verify Score		0.66	0.18	0.18	0.89	0.89		
PSI- BLAST		0	5.1e-36	5.1e-36	9.1e-29	9.1e-29	9.1e-29	9.1e-29
End		792	322	322	170	170	170	170
Start AA		201	177	177	25	55	55	55
Chain D		m	Ą	¥				
PDB CD		1djx	lexr	lexr	lmai	Imai	lmai	lmai
SEQ No. u		121	121	121	121	121	121	121

PDB annotation	CALCIUM-BINDING PROTEIN EF- HAND 1TNX 14	CALCIUM-BINDING PROTEIN BF- HAND 1TNX 14			CALMODULIN, CALCIUM BINDING, HELIX-LOOP-HELIX, SIGNALLING, 2 COMPLEX(CALCIUM-BINDING PROTEIN/PEPTIDE)	CALMODULIN, CÁLCIUM BINDING, HELIX-LOOP-HELIX, SIGNALLING, 2 COMPLEX(CALCIUM-BINDING PROTEIN/PEPTIDE)		IMMUNOGLOBULIN IMMUNOGLOBULIN	CATALYTIC ANTIBODY CATALYTIC ANTIBODY. ESTERASE	COMPLEX (IMMUNOGLOBULIN/VIRAL PEPTIDE) ANTIBODY '8F5; IMMUNOGLOBULIN, ANTIBODY, RHINOVIRUS, NEUTRALIZATION, 2 CONTINUOUS EPITOPE, COMPLEX (IMMUNOGLOBULIN/VIRAL PEPTIDE)
Coumpound	TROPONIN C; ITNX 4 CHAIN: NULL; ITNX 5	TROPONIN C; 1TNX 4 CHAIN: NULL; 1TNX 5	CONTRACTILE SYSTEM PROTEIN TROPONIN C 1TOP 3	CONTRACTILE SYSTEM PROTEIN TROPONIN C 1TOP 3	CALMODULIN; CHAIN: A; RS20; CHAIN: B;	CALMODULIN; CHAIN: A; RS20; CHAIN: B;		2E8 (IGG1=KAPPA=) ANTIBODY; CHAIN: L, H, M, P;	29G11 FAB; CHAIN: L, H;	IGG2A; CHAIN: L, H; HUMAN RHINOVIRUS CAPSID PROTEIN VP2; CHAIN: P;
SeqFold Score								64.22	63.99	68.09
PMF Score	0.09	60.0	0.84	0.84	0.33	0.33				
Verify Score	0.07	0.07	0.26	0.26	0.07	0.07				
PSI- BLAST	3.4e-34	3.4e-34	1.4e-34	1.4e-34	3.4e-36	3.4e-36	;	5.1e-27	5.1e-24	1.5e-27
End AA	320	320	320	320	323	323	ļ	247	245	247
Start AA	179	179	179	179	176	176		35	40	40
Chain ID					A	V		Ľ.	н	н
PDB ID	ltmx	ltnx	ltop	ltop	lvrk	lvrk	+		1а0q	1a3r
SEQ NO BEG	121	121	121	121	121	121		771	122	122

PDB annotation	COMPLEX (IMMUNOGLOBULIN/VIRAL PEPTIDE) ANTIBODY 8F5; IMMUNOGLOBULIN, ANTIBODY, RHINOVIRUS, NEUTRALIZATION, 2 CONTINUOUS EPITOPE, COMPLEX (IMMUNOGLOBULIN/VIRAL PEPTIDE)	IMMUNOGLOBULIN IMMUNOGLOBULIN, FAB, ANTIBODY, ANTI-E-SELECTIN	IMMUNOGLOBULIN IMMUNOGLOBULIN, FAB FRAGMENT, HUMANISATION	IMMUNOGLOBULIN IMMUNOGLOBULIN, C REGION, V REGION	IMMUNOGLOBULIN IMMUNOGLOBULIN, ANTIBODY FAB', CATALYST, ALDOLASE REACTION	IMMUNOGLOBULIN IMMUNOGLOBULIN, ANTIBODY, FAB, ENZYME INHIBITOR, PCR, 2 HOT START	·
Coumpound	IGG2A; CHAIN: L, H; HUMAN RHINOVIRUS CAPSID PROTEIN VP2; CHAIN: P;	MONOCLONAL ANTI-B-SELECTIN 7A9 ANTIBODY; CHAIN: L, H;	ANTIBODY CTM01; CHAIN: L, H;	ANTI-IDIOTYPIC FAB 409.5.3 (IGG2A) FAB; CHAIN: A, B, L, H	IMMUNOGLOBULIN IGG2A; CHAIN: L, H;	TP7 FAB; CHAIN: L, H;	IMMUNOGLOBULIN FAB FRAGMENT OF MURINE MONOCLONAL ANTIBODY AN02 COMPLEX 1BAF 3 WITH ITS HAPTEN
SeqFold Score	,	63.45	63.32		65.91	67.40	63.28
PMF	0.48			0.42			
Verify Score	0.10			-0.20			
PSI- BLAST	1.5e-27	1.7e-25	6.8e-25	le-17	5.1e-27	1e-26	1e-24
End AA	242	245	245	231	247	247	247
Start AA	41	39	35	37	37	35	35
Chain D	н	Н	н	1	н	H	н
FDB EDB	1a3r	la5f	lae6	laif	laxt	layl	lbaf
SEQ S D	122	122	122	122	122	122	122

PDB annotation		COMPLEX (ANTIBODY/PEPTIDE) POLYSPECIFICITY, CROSS REACTIVITY, FAB-FRAGMENT, PEPTIDE, 2 HIV-1, COMPLEX (ANTIBODY/PEPTIDE)		ANTIBODY, CD52	CATALYTIC ANTIBODY CATALYTIC ANTIBODY, TERPENOID SYNTHASE, CARBOCATION, 2 CYCLIZATION CASCADE	CATALYTIC ANTIBODY CATALYTIC ANTIBODY,
Coumpound	(2,2,6,6- TETRAMETHYL-1- PIPERIDINYLOXY- 1BAF 4 DINITROPHENYL)	ANTIBODY (CB 4-1); CHAIN: A, B; PEPTIDE; CHAIN: C;	COMPLEX (ANTIBODY/ANTIGE N) HYHEL-5 FAB COMPLEXED WITH BOBWHITE QUAIL LYSOZYME 1BQL 3 1BOL 95	CAMPATH- IH:LIGHT CHAIN; CHAIN: L; CAMPATH- IH:HEAVY CHAIN; CHAIN: H; PEPTIDE ANTIGEN: CHAIN: P:	CATALYTIC ANTIBODY 19A4 (LIGHT CHAIN); CHAIN: L; CATALYTIC ANTIBODY 19A4 (HEAVY CHAIN);	CATALYTIC ANTIBODY 19A4
SeqFold Score		64.40	64.73		64.05	
PMF Score				0.34		0.16
Verify Score				0.09		0.08
PSI- BLAST		3.4e-24	3.4e-24	1.5e-27	5.1e-27	5.1e-27
End AA		247	246	242	247	242
Start AA		35	36	37	33	4
Chain D		В	н	Ħ	ж	н
PDB ID		lbog.	1bq1	lce1	1cf8	1cf8
SEQ Più Più		122	122	122	122	122

PDB annotation	TERPENOID SYNTHASE, CARBOCATION, 2 CYCLIZATION CASCADE	CATALYTIC ANTIBODY CATALYTIC ANTIBODY, TERPENOID SYNTHASE, CARBOCATION, 2 CYCLIZATION CASCADE	IMMUNE SYSTEM ANTI-PRION FAB 3F4; ANTI-PRION FAB 3F4 ANTI- PRION ANTIBODY, FAB 3F4	IMMUNE SYSTEM ABZYME TRANSITION STATE ANALOG, IMMUNE SYSTEM	IMMUNE SYSTEM ANTI-LYSOZYME ANTIBODY, HYHEL-63, HEN EGG WHITE LYSOZYME	IMMUNOGLOBULIN FAB, ANTIBODY, ANTIGEN, HIV-1, P24,
Coumpound	(LIGHT CHAIN); CHAIN: L; CATALYTIC ANTBODY 19A4 (HBAVY CHAIN); CHAIN: H;	CATALYTIC ANTIBODY 19A4 (LIGHT CHAIN); CHAIN: L; CATALYTIC ANTIBODY 19A4 (HEAVY CHAIN);	FAB ANTIBODY LIGHT CHAIN; CHAIN: L; FAB ANTIBODY HEAVY CHAIN; CHAIN: H;	7C8 FAB FRAGMENT; SHORT CHAIN; CHAIN: A, C; 7C8 FAB FRAGMENT; LONG CHAIN; CHAIN: B, D	ANTI-LYSOZYME ANTIBODY HYHEL- 63 (LIGHT CHAIN); CHAIN: A, C; ANTI- LYSOZYME ANTIBODY HYHEL- 63 (HEAVY CHAIN); CHAIN: B, D;	IMMUNOGLOBULIN LIGHT CHAIN;
SeqFold Score				62.70		
PMF Score		0.31	0.57		0.07	0.06
Verify Score		-0.19	0.20		-0.13	-0.17
PSI- BLAST		1.46-17	6.8e-30	3.46-24	6.8e-28	8.5e-18
End		231	242	247		231
Start AA		40	41	37	4	40
Chain ID		L)	н	B	В	L
PDB ID		1cf8	lcr9	1ct8	1dqq	1e60
S E S E S		122	122	122	122	122

PDB annotation	CA	VIRUS/VIRAL PROTEIN RECEPTOR IMMUNOGLOBULIN V DOMAIN FOLD, SYMMETRIC DIMER	VIRUS/VIRAL PROTEIN RECEPTOR IMMUNOGLOBULIN V DOMAIN FOLD, SYMMETRIC DIMBR		IMMUNE SYSTEM VON WILLEBRAND FACTOR, GLYCOPROTEIN IBA (A:ALPHA) BINDING, 2 COMPLEX (WILLEBRAND/IMMUNOGLOBULIN), BLOOD COAGULATION TYPE 3 2B VON WILLEBRAND DISEASE	IMMUNE SYSTEM BET V I-A, BETVI ALLERGEN; BV16 FAB-FRAGMENT, KAPPA MOPC21 CODING SEQUENCE, HEAVY CHAIN OF THE MONOCLONAL ANTIBODY MST2; BET V 1, BV16 FAB FRAGMENT, ANTIBODY ALLERGEN COMPLEX
Coumpound	CHAIN: L; IMMUNOGLOBULIN HEAVY CHAIN; CHAIN: H;	COXSACKIE VIRUS AND ADENOVIRUS RECEPTOR; CHAIN: A, B;	COXSACKIE VIRUS AND ADENOVIRUS RECEPTOR; CHAIN: A, B;	IMMUNOGLOBULIN IMMUNOGLOBULIN GI (KAPPA LIGHT CHAIN) FAB' FRAGMENT 1FIG 3	IMMUNOGLOBULIN NMC-4 IGG1; CHAIN: L; IMMUNOGLOBULIN NMC-4 IGG1; CHAIN: H; VON WILLEBRAND FACTOR; CHAIN: A;	MAJOR POLLEN ALLERGEN BET V 1- A; CHAIN: A, D, G, J; IMMUNOGLOBULIN KAPPA LIGHT CHAIN; CHAIN: B, E, H, K; ANTIBODY HEAVY CHAIN FAB; CHAIN: C, F, I, L;
SeqFold Score				71.28		
PMF Score		0.98	0.92		0.06	0.00
Verify Score		0.36	0.22		-0.07	0.03
PSI- BLAST		1.3e-24	3.4e-22	-8.5e-24	1.7e-18	le-17
End AA		150	152	244	231	231
Start AA	·	35	37	35	37	41
Chain TO	·	A	¥	Н	J	æ
PDB CD		1f5w	1f5w	lfig	1fms	1fsk
ge e ë		122	122	122	122	152

				_		
PDB annotation	ANTIBODY FAB FRAGMENT ANTIBODY FAB FRAGMENT	IMMUNOGLOBULIN PROTEIN ENGINEERING, ANTIBODY DESIGN, IMMUNOGLOBULIN 2 STRUCTURE, ANTIGEN-BINDING SITE, CANONICAL CONFORMATION, 3 COMPLEMENTARITY- DETERMINING REGION		COMPLEX (IMMUNOGLOBULIN/RECEPTOR) TCR VAPLHA VBETA DOMAIN; T- CELL RECEPTOR, STRAND SWITCH, FAB, ANTICLONOTYPIC, 2 (IMMUNOGLOBULIN/RECEPTOR)	COMPLEX (IMMUNOGLOBULIN/RECEPTOR) TCR VAPLHA VBETA DOMAIN; T- CELL RECEPTOR, STRAND SWITCH, FAB, ANTICLONOTYPIC, 2 (IMMUNOGLOBULIN/RECEPTOR)	
Coumpound	ANTI-ANTI- IDIOTYPE GH1002 FAB FRAGMENT; CHAIN: L, H	ANTIBODY M41; CHAIN: L, H, M, I;	IMMUNOGLOBULIN FAB (IGG2A,KAPPA) FRAGMENT (26-10) COMPLEX WITH DIGOXIN IIGJA 1	KB5-C20 T-CELL ANTIGEN RECEPTOR; CHAIN: A, B; ANTIBODY DESIRE-1; CHAIN: L,	KB5-C20 T-CELL ANTIGEN RECEPTOR; CHAIN: A, B; ANTIBODY DESIRE-1; CHAIN: L,	IMMUNOGLOBULIN FAB FRAGMENT (MURINE SE155-4) COMPLEX WITH DODECASACCHARI DE 1MFE 3 {-
SeqFold Score	66.93		65.63	68.30		64.30
PMF Score		-0.09			0.88	
Verify Score		0.04			0.15	
PSI- BLAST	1.7e-23	1.7e-28	1.7e-22	6.8e-25	1.7e-19	1.5e-22
End AA	245	242	246	247	231	247
Start AA	40	4	36	35	37	37
Chain ID	н	H	В	н	٦	Н
808 CD	1ghf	1gpo	1igi	1kb5	1kb5	1mfe
SEQ B G S	122	122	122	122	122	122

PDB annotation		IMMUNOGLOBULIN FAB FRAGMENT, IMMUNOGLOBULIN	COMPLEX (IMMUNOGLOBULIN/HYDROLASE) N10 FAB IMMUNOGLOBULIN; INSN 7 STAPHYLOCOCCAL NUCLEASE RIBONUCLEATE, INSN 11 IMMUNOGLOBULIN, STAPHYLOCOCCAL NUCLEASE INSN 25	IMMUNOGLOBULIN FAB, GD2-GANGLIOSIDE, CARBOHYDRATE, MELANOMA, IMMUNOGLOBULIN	COMPLEX (ANTIBODY/PEPTIDE EPITOPE) ANTIBODY, PEPTIDE ANTIGEN, ANTITUMOR ANTIBODY, 2 COMPLEX (ANTIBODY/PEPTIDE EPITOPE)	COMPLEX (ANTIBODY/PEPTIDE EPITOPE) ANTIBODY, PEPTIDE ANTIGEN, ANTITUMOR ANTIBODY,
Coumpound	3)ALPHA-D-GALACTOSE(1- 2)[ALPHA-D-ABEQUOSE(1- 3)]ALPHA- 1MFE 4 D-MANNOSE(1- 4)ALPHA-L-RHAMNOSE(1-} (PART OF THE 1MFE 5 CELL SURFACE CARBOHYDRATE OF PATHOGENIC SALMONELLA) 1MFE 6	FAB1583; CHAIN: L, H	IGG FAB (IGG1, KAPPA); INSN 4 CHAIN: L, H; INSN 5 STAPHYLOCOCCAL NUCLEASE; INSN 9 CHAIN: S; INSN 10	ANTIBODY; CHAIN: L, H;	SM3 ANTIBODY; CHAIN: L, H; PEPTIDE EPITOPE; CHAIN: P;	SM3 ANTIBODY; CHAIN: L, H; PEPTIDE EPITOPE;
SeqFold Score		68.87	63.71	62.61	63.77	ļ
PMF Score	·					0.35
Verify Score						0.00
PSI. BLAST		1.2e-26	1.7e-26	5.1e-23	6.8e-29	6.8e-29
End AA		246	244	240	247	242
Start AA		35	39	35	35	37
Chain ID		Н	н	H	н	Н
PDB TD		1nld	Insn	1psk	1sm3	lsm3
SEQ EQ EQ		122	122	122	122	122

РDВ annotation	2 COMPLEX (ANTIBODY/PEPTIDE EPITOPE)		COMPLEX (ANTIBODY/ELECTRON TRANSPORT) FAB E8; CYT C, ANTIGEN; IMMUNOGLOBULIN, IGG1 KAPPA, FAB FRAGMENT, HORSE 2 CYTOCHROME C, COMPLEX (ANTIBODY/ELECTRON TRANSPORT)	COMPLEX (ANTIBODY/ELECTRON TRANSPORT) FAB E8; CYT C, ANTIGEN; IMMUNOGLOBULIN, IGG1 KAPPA, FAB FRAGMENT, HORSE 2 CYTOCHROME C, COMPLEX (ANTIBODY/ELECTRON TRANSPORT)	CATALYTIC ANTIBODY CATALYTIC ANTIBODY, FAB, RING CLOSURE REACTION	
Coumpound	CHAIN: P;	IMMUNOGLOBULIN IGG1 MONOCLONAL FAB FRAGMENT (TE33) COMPLEX WITH CHOLERA 1TET 3 TOXIN PEPTIDE 3 (CTP3)	E8 ANTIBODY; CHAIN: L, H; CYTOCHROME C; CHAIN: F;	E8 ANTIBODY; CHAIN: L, H; CYTOCHROME C; CHAIN: F;	IGG 5C8; CHAIN: L, H;	COMPLEX(ANTIBOD Y-ANTIGEN) IG*G1 FAB FRAGMENT (HY/HEL\$-10) AND LYSOZYME (E.C.3.2.1.17) 3HFM 4 COMPLEX 3HFM 5
SeqFold Score		62.73	66.09		71.71	65.83
PMF Score				0.81		
Verify Score				-0.30		
PSI- BLAST		6.8e-25	1.7e-25	8.5e-19	1.2e-26	1.4e-28
End AA		247	253	231	245	247
Start AA		35	35	37	35	35
Chain ID		н	н	ı	н	н
PDB TD		ltet	Iwej	lwej	25c8	3hfm
SEQ D No:		122	122	122	122	122

PDB annotation		TRANSCRIPTION COOA GENE PRODUCT; CARBON MONOXIDE, HEME SENSOR, CATABOLITE GENE ACTIVATOR 2 PROTEIN	TRANSCRIPTION COOA GENE PRODUCT; CARBON MONOXIDE, HEME SENSOR, CATABOLITE GENE ACTIVATOR 2 PROTEIN	KINASE RI(ALPHA); REGULATORY SUBUNIT, KINASE	TRANSCRIPTION/DNA COMPLEX (TRANSCRIPTION REGULATION/DNA), DNA-BINDING, CAMP- 2 BINDING, ACTIVATOR	
Coumpound	COMPLEX(ANTIBOD Y-ANTIGEN) IG*G1 FAB FRAGMENT (HY/HEL\$-10) AND LYSOZYME (E.C.3.2.1.17) 3HFM 4 COMPLEX 3HFM 5	CARBON MONOXIDE OXIDATION SYSTEM TRANSCRIPTION CHAIN: A, B;	CARBON MONOXIDE OXIDATION SYSTEM TRANSCRIPTION CHAIN: A, B;	CAMP DEPENDENT PROTEIN KINASE; CHAIN: NULL;	CATABOLITE GENE ACTIVATOR PROTEIN; CHAIN: A; DNA (5'- D(*GP*TP*CP*AP*C P*AP*TP*TP*AP*AP *T)-3'); CHAIN: B; DNA (5'- CHAIN: C;	HYDROLASE(O- GLYCOSYL)
SeqFold Score						
PMF	0.28	0.06	0.05	0.62	0.23	1.00
Verify Score	0.00	-0.08	-0.21	0.33	-0.25	0.70
PSI- BLAST	1.4e-28	2.6e-06	3.4e-05	1.4e-27	1.7e-26	1e-47
End	242	303	319	288	319	212
Start AA	4	176	181	135	171	36
Chain	H	<	4		∀	
PDB CI	3hfm	1169	149	lrgs	2cgp	1531
S a S	122	123	123	123	123	127

PDB annotation						GLYCOPROTEIN MEMBRANE COFACTOR PROTEIN (MCP); VIRUS RECEPTOR, COMPLEMENT COFACTOR, SHORT CONSENSUS REPEAT, 2 SCR, MEASLES VIRUS, GLYCOPROTEIN	GLYCOPROTEIN MEMBRANE COFACTOR PROTEIN (MCP); VIRUS RECEPTOR, COMPLEMENT COFACTOR, SHORT CONSENSUS REPEAT, 2 SCR, MEASLES VIRUS, GLYCOPROTEIN	GLYCOPROTEIN MEMBRANE COFACTOR PROTEIN (MCP); VIRUS RECEPTOR, COMPLEMENT COFACTOR, SHORT CONSENSUS REPEAT, 2 SCR, MEASLES VIRUS, GLYCOPROTEIN	GLYCOPROTEIN MEMBRANE
Coumpound	LYSOZYME (E.C.3.2.1.17) 153L 3	HYDROLASE(O-GLYCOSYL) LYSOZYME (E.C.3.2.1.17) 153L 3	HYDROLASE(O- GLYCOSYL) LYSOZYME (E.C.3.2.1.17) 153L 3	HYDROLASE(O- GLYCOSYL) LYSOZYME (E.C.3.2.1.17) 153L 3		CD46; CHAIN: A, B, C, D, E, F,	CD46; CHAIN: A, B, C, D, E, F,	CD46; CHAIN: A, B, C, D, E, F;	CD46; CHAIN: A, B,
SeqFold Score			186.19	186.19					58.04
PMF Score		1.00				0.87	-0.15	1.00	
Verify Score		0.70				0.10	0.05	0.40	
PSI- BLAST		1e-47	1e-47	1e-47		2.6e-11	5.1e-18	Ie-18	le-18
End		212	212	212		267	145	201	204
Start AA		36	36	36	1	147	29		87
Chain ID						A	¥	¥	A
PDB ID		1531	1531	1531		1cki	1cki	1ckl	1cki
SEQ B B SE		127	127	127		128	128	128	128

PDB annotation	COFACTOR PROTEIN (MCP); VIRUS RECEPTOR, COMPLEMENT COFACTOR, SHORT CONSENSUS REPEAT, 2 SCR, MEASLES VIRUS, GLYCOPROTEIN	COMPLEMENT INHIBITOR VCP, SP35; COMPLEMENT, NMR, MODULES, PROTEIN STRUCTURE, VACCINIA VIRUS	COMPLEMENT INHIBITOR VCP, SP35; COMPLEMENT, NMR, MODULES, PROTEIN STRUCTURE, VACCINIA VIRUS	COMPLEMENT INHIBITOR VCP, SP35; COMPLEMENT, NMR, MODULES, PROTEIN STRUCTURE, VACCINIA VIRUS			
Coumpound	C, D, B, F;	COMPLEMENT CONTROL PROTEIN; CHAIN: A;	COMPLEMENT CONTROL PROTEIN; CHAIN: A;	COMPLEMENT CONTROL PROTEIN; CHAIN: A;	GLYCOPROTEIN 16TH COMPLEMENT CONTROL PROTEIN (/CCP\$) OF FACTOR H 1HCC 3	GLYCOPROTEIN 16TH COMPLEMENT CONTROL PROTEIN (/CCP\$) OF FACTOR H 1HCC3	GLYCOPROTEIN FACTOR H, 15TH AND 16TH C. MODULE PAIR (NMR, MINIMIZED 1HFHA 1
SeqFold Score							
PMF Score		0.65	1.00	86.0	1.00	0.90	0.52
Verify Score		0.19	0.65	0.43	0.55	0.44	0.19
PSI- BLAST		1.7e-15	7.8e-25	1.4e-24	6.5e-16	1.3e-10	3.4e-14
End AA		141	201	202	202	141	266
Start AA		29	<i>L</i> 8	<i>L</i> 8	147	87	143
Chain D		Ą	A	Ą			
PDB CO		1e5g	1e5g	1e5g	lhcc	lhcc	1hfh
SEQ No u		128	128	128	128	128	128

PDB annotation																										
Coumpound	STRUCTURE) 1HFH 4 1HFHA 5	GLYCOPROTEIN FACTOR H, 15TH AND 16TH C-	MODULE PAIR	(NMR, MINIMIZED	AVERAGED	STRUCTURE) 1HFH 4 1HFHA 5	GLYCOPROTEIN	FACTOR H, 15TH	AND 16TH C.	MODULE PAIK	IHFHA 1	AVERAGED	STRUCTURE) 1HFH 4 1HFHA 5	GLYCOPROTEIN	FACTOR H, 15TH	AND 16TH C-	MODULE PAIR	(NMR, MINIMIZED	AVEDAGED	STRIICTURE) 1HFH 4	1HFHA 5	GLYCOPROTEIN	FACTOR H, 15TH C-	MODULE PAIR	(NMR, MINIMIZED	AVERAGED IHFIA 1 STRUCTURE) 1HFI 4
SeqFold Score							93.95																			
PMF Score		0.05		_										0.82								96.0				
Verify Score		0.19												0.28								99.0				
PSI- BLAST		1.7e-13					3.4e-17							3.4e-17	1							3.9e-16				
End AA		141					202							202					-			201	-			
Start AA		78					83	·						28								147				
Chain ID																										
PDB CD		1hfh					1hfh							1hfh								1hfi				
S e S		128					128							128								128				

PDB annotation			COMPLEX (BLOOD COAGULATION/INHIBITOR) CHRISTMAS FACTOR; COMPLEX, INHIBITOR, HEMOPHILIA/EGF,	BLOOD COAGULATION, 2 PLASMA, SERINE PROTEASE, CALCIUM- BINDING, HYDROLASE, 3 GLYCOPROTEIN	MEMBRANE ADHESION SHORT CONSENSUS REPEAT, SUSHI,	COMPLEMENT CONTROL PROTEIN, 2 N-GLYCOSYLATION, MULTI-	MEMBRANE ADHESION SHORT	CONSENSUS REPEAT, SUSHI, COMPLEMENT CONTROL PROTEIN,	2 N-GLYCOSYLATION, MULTI- DOMAIN, MEMBRANE ADHESION	COMPLEMENT INHIBITOR SP35,	VCP, VACCINIA VIRUS SP35; COMPLEMENT INHIBITOR,	COMPLEMENT MODULE, SCR,	SUSHI DOMAIN, 2 MODULE PAIR	COMPLEMENT INHIBITOR SP35, VCP VACCINIA VIRTIS SP35.	COMPLEMENT INHIBITOR,
Coumpound	IHFIA 5	GLYCOPROTEIN FACTOR H, 15TH C- MODULE PAIR (NMR, MINIMIZED AVERAGED 1HFIA 1 STRUCTURE) 1HFI 4	FACTOR IXA; CHAIN: C, L.; D-PHE- PRO-ARG; CHAIN: I;		HUMAN BETA2- GLYCOPROTEIN I;	CHAIN: A;	HUMAN BETA2-	GLYCOPROTEIN I; CHAIN: A;		VACCINIA VIRUS	COMPLEMENT CONTROL PROTEIN;	CHAIN: NULL;		VACCINIA VIRUS	CONTROL PROTEIN;
SeqFold Score					95.32										
PMF Score		1.00	0.10				0.87			0.21		•	,	-0.05	
Verify Score		0.57	0.15				0.07		•	-0.22				0.07	
PSI- BLAST		5.26-10	5.1e-10		6.8e-39		6.8e-39		•	3.4e-24			,	1.5e-17	
End		140	192		266		266			790			,	142	
Start AA		87	104		3		∞			145				83	
Chain ID			ı		Ą		V								
PDB ID		1116	1pfx		1qub		1qub			lvvc	_			Iwc	
SEQ DD NO:		128	128		128		128			128				128	

	·			_			
PDB annotation	COMPLEMENT MODULE, SCR, SUSHI DOMAIN, 2 MODULE PAIR	COMPLEMENT INHIBITOR SP35, VCP, VACCINIA VIRUS SP35; COMPLEMENT INHIBITOR, COMPLEMENT MODULE, SCR, SUSHI DOMAIN, 2 MODULE PAIR	COMPLEMENT INHIBITOR SP35, VCP, VACCINIA VIRUS SP35; COMPLEMENT INHIBITOR, COMPLEMENT MODULE, SCR, SUSHI DOMAIN, 2 MODULE PAIR			COMPLEX (BLOOD COAGULATION/INHIBITOR) AUTOPROTHROMBIN IIA; HYDROLASE, SERINE PROTEINASE), PLASMA CALCIUM BINDING, 2 GLYCOPROTEIN, COMPLEX (BLOOD COAGULATION/INHIBITOR)	BLOOD COAGULATION, SERINE PROTEASE, COMPLEX, CO-FACTOR, 2 RECEPTOR ENZYME, INHIBITOR, GLA, EGF, 3 COMPLEX (SERINE
Coumpound	CHAIN: NULL;	VACCINIA VIRUS COMPLEMENT CONTROL PROTEIN; CHAIN: NULL;	VACCINIA VIRUS COMPLEMENT CONTROL PROTEIN; CHAIN: NULL;		PROTEINASE INHIBITOR(TRYPSIN) TRYPSIN INHIBITOR (PH 4.75) 1ATA 3 (NMR, MINIMIZED AVERAGE STRUCTURE) 1ATA	ACTIVATED PROTEIN C; CHAIN: C, L; D-PHE-PRO- MAI; CHAIN: P;	BLOOD COAGULATION FACTOR VIIA; CHAIN: L, H;
SeqFold Score		82.91					
PMF Score			1.00		0.09	-0.19	-0.18
Verify Score			0.30		0.29	0.29	0.49
PSI- BLAST		3.4e-20	3.4e-20		5.2e-12	5.16-11	1.7e-10
End		203	202		968	940	868
Start		98	87		834		819
Chain						ы	ı
PDB ID		lwc	lvvc		lata	laut	1dan
SEQ B B		128	128		129	129	129

PDB annotation	PROTEASE/COFACTOR/LIGAND)	BLOOD COAGULATION, SERINE PROTEASE, COMPLEX, CO-FACTOR, 2 RECEPTOR ENZYME, INHIBITOR, GLA, EGF, 3 COMPLEX (SERINE PROTEASE/COFACTOR/LIGAND)	BLOOD COAGULATION, SERINE PROTEASE, COMPLEX, CO-FACTOR, 2 RECEPTOR ENZYME, INHIBITOR, GLA, EGF, 3 COMPLEX (SERINE PROTEASE/COFACTOR/LIGAND)	HYDROLASE/HYDROLASE INHIBITOR PROTEIN-PEPTIDE COMPLEX
Coumpound	SOLUBLE TISSUE FACTOR; CHAIN: T, U; D-PHE-PHE-ARG- CHLOROMETHYLKE TONE (DFFRCMK)	BLOOD COAGULATION FACTOR VIIA; CHAIN: L, H; SOLUBLE TISSUE FACTOR; CHAIN: T, U; D-PHE-PHE-ARG- CHLOROMETHYLKE TONE (DFFRCMK) WITH CHAIN: C;	BLOOD COAGULATION FACTOR VIIA; CHAIN: L, H; SOLUBLE TISSUE FACTOR; CHAIN: T, U; D-PHE-PHE-ARG- CHLOROMETHYLKE TONE (DFFRCMK) WITH CHAIN: C;	DES-GLA FACTOR VIIA (HEAVY CHAIN); CHAIN: H, I; DES-GLA FACTOR VIIA (LIGHT CHAIN); CHAIN: L, M; (DPN)- PHE-ARG; CHAIN: C, D; PEPTIDE E-76; CHAIN: X, Y;
SeqFold Score			·	
PMF Score		-0.15	-0.18	-0.18
Verify Score		0.08	0.01	0.20
PSI- BLAST		3.4e-12	1.7e-10	8.5e-14
End AA		943	1020	427
Start AA		851	939	330
Chain ID		T	I	L)
PDB ID		1dan	ldan	ldva
SEQ NO ID		129	129	129

PDB annotation	HYDROLASE/HYDROLASE INHIBITOR PROTEIN-PEPTIDE COMPLEX	HYDROLASE/HYDROLASE INHIBITOR PROTEIN-PEPTIDE COMPLEX	SERINE PROTEINASE COAGULATION FACTOR II; COAGULATION FACTOR II; FETOMODULIN, TM, CD141 ANTIGEN; EGR-CMK SERINE PROTEINASE, EGF-LIKE DOMAINS, ANTICOAGULANT COMPLEX, 2 ANTIFIBRINOLYTIC COMPLEX	SERINE PROTEINASE COAGULATION FACTOR II; COAGULATION FACTOR II; FETOMODULIN, TM, CD141 ANTIGEN; EGR-CMK SERINE PROTEINASE, EGF-LIKE DOMAINS,
Coumpound	DES-GLA FACTOR VIIA (HEAVY CHAIN); CHAIN: H, I; DES-GLA FACTOR VIIA (LIGHT CHAIN); CHAIN: L, M; (DPN)- PHE-ARG; CHAIN: C, D; PEPTIDE E-76; CHAIN: X, Y;	DES-GLA FACTOR VIIA (HEAVY CHAIN); CHAIN: H, I; DES-GLA FACTOR VIIA (LIGHT CHAIN); CHAIN: L, M; (DPN)- PHE-ARG; CHAIN: C, D; PEPTIDE E-76; CHAIN: X, Y;	THROMBIN LIGHT CHAIN; CHAIN: A, B, C, D; THROMBIN HEAVY CHAIN; CHAIN: M, N, O, P; THROMBOMODULI N; CHAIN: I, J, K, L; THROMBIN INHIBITOR L-GLU-L- GLY-L-ARM; CHAIN: E, F, G, H;	THROMBIN LIGHT CHAIN; CHAIN: A, B, C, D; THROMBIN HEAVY CHAIN; CHAIN: M, N, O, P; THROMBOMODULI
SeqFold Score				
PMF Score	-0.12	-0.14	-0.20	-0.20
Verify Score	0.65	0:30	0.02	0.02
PSI- BLAST	1.7e-10	3.4e-12	3.4e-11	3.4e-11
End AA	868	943	1294	1294
Start AA	819	851	1167	1167
Chain ID	1	٦	—	П
PDB ID	ldva	1dva	1dx5	1dx5
SEQ No B	129	129	129	129

PDB annotation	ANTIFIBRINOLYTIC COMPLEX, 2 ANTIFIBRINOLYTIC COMPLEX	BLOOD CLOTTING COMPLEX(SERINE PROTEASE/COFACTOR/LIGAND), BLOOD COAGULATION, 2 SERINE PROTEASE, COMPLEX, CO-FACTOR, RECEPTOR ENZYME, 3 INHIBITOR, GLA, EGF, COMPLEX (SERINE 4 PROTEASE/COFACTOR/LIGAND), BLOOD CLOTTING	BLOOD CLOTTING COMPLEX(SERINE PROTEASE/COFACTOR/LIGAND), BLOOD COAGULATION, 2 SERINE PROTEASE, COMPLEX, CO-FACTOR, RECEPTOR ENZYME, 3 INHIBITOR, GLA, EGF, COMPLEX (SERINE 4 PROTEASE/COFACTOR/LIGAND), BLOOD CLOTTING	BLOOD CLOTTING COMPLEX(SERINE PROTEASE/COFACTOR/LIGAND), BLOOD COAGULATION, 2 SERINE PROTEASE, COMPLEX, CO-FACTOR, RECEPTOR ENZYME, 3 INHIBITOR, GLA, EGF, COMPLEX (SERINE 4 PROTEASE/COFACTOR/LIGAND), BLOOD CLOTTING
Coumpound	N; CHAIN: I, I, K, L; THROMBIN INHIBITOR L-GLU-L- GLY-L-ARM; CHAIN: E, F, G, H;	BLOOD COAGULATION FACTOR VIIA; CHAIN: L; BLOOD COAGULATION FACTOR VIIA; CHAIN: H; SOLUBLE TISSUE FACTOR; CHAIN: T; 5L15; CHAIN: I;	BLÖOD COAGULATION FACTOR VIIA; CHAIN: L; BLOOD COAGULATION FACTOR VIIA; CHAIN: H; SOLUBLE TISSUE FACTOR; CHAIN: T; 5L15; CHAIN: I;	BLOOD COAGULATION FACTOR VIIA; CHAIN: L; BLOOD COAGULATION FACTOR VIIA; CHAIN: H; SOLUBLE TISSUE FACTOR; CHAIN: T; 5L15; CHAIN: I;
SeqFold Score				
PMF		-0.18	-0.18	-0.14
Verify Score		0.27	0.27	0.05
PSI- BLAST		1.7e-10	1.7e-10	3.4e-12
End AA		868	868	943
Start AA		819	819	851
Chain		H	ы	ı
PDB ID		1fak	1fak	1fak
SEQ B B		129	129	129

							
PDB annotation	BLOOD CLOTTING COMPLEX(SERINE PROTEASE/COFACTOR/LIGAND), BLOOD COAGULATION, 2 SERINE PROTEASE, COMPLEX, CO-FACTOR, RECEPTOR ENZYME, 3 INHIBITOR, GLA, EGF, COMPLEX (SERINE 4 PROTEASE/COFACTOR/LIGAND), BLOOD CLOTTING	GLYCOPROTEIN GLYCOPROTEIN	GLYCOPROTEIN GLYCOPROTEIN	GLYCOPROTEIN GLYCOPROTEIN	COMPLEX (BLOOD COAGULATION/NHIBITOR) CHRISTMAS FACTOR; COMPLEX, NHIBITOR, HEMOPHILIA/EGF, BLOOD COAGULATION, 2 PLASMA, SERINE PROTEASE, CALCIUM- BINDING, HYDROLASE, 3 GLYCOPROTEIN	COMPLEX (BLOOD COAGULATION/INHIBITOR) CHRISTMAS FACTOR; COMPLEX, INHIBITOR, HEMOPHILIA/EGF, BLOOD COAGULATION, 2 PLASMA, SERINE PROTEASE, CALCIUM- BINDING, HYDROLASE, 3 GLYCOPROTEIN	COMPLEX (BLOOD COAGULATION/INHIBITOR)
Coumpound	BLOOD COAGULATION FACTOR VIIA; CHAIN: L; BLOOD COAGULATION FACTOR VIIA; CHAIN: H; SOLUBLE TISSUE FACTOR; CHAIN: T; 5L15; CHAIN: I;	LAMININ; CHAIN: NULL;	LAMININ; CHAIN: NULL;	LAMININ; CHAIN: NULL;	FACTOR IXA; CHAIN: C, L.; D-PHE- PRO-ARG; CHAIN: I;	FACTOR IXA; CHAIN: C, L.; D-PHE- PRO-ARG; CHAIN: 1;	FACTOR IXA; CHAIN: C, L.; D-PHE-
SeqFold Score							
PMF Score	-0.15	-0.15	-0.18	-0.18	-0.14	-0.18	-0.19
Verify Score	0.10	0.21	0.20	0.20	0.15	0.03	60:0
PSI- BLAST	3.4e-12	1e-09	3.4e-15	3.4e-15	1.4e-10	2.6e-08	1.7e-09
End	943	472	905	206	438	920	868
Start AA	851	333	755	755	330	277	819
Chain	ы					<u>ب</u>	L L
FDB CD	1fak	1klo	1klo	1klo	1pfx	1pfx	1pfx
SEQ ES	129	129	129	129	129	129	129

PDB annotation	CHRISTMAS FACTOR; COMPLEX, INHIBITOR, HEMOPHILIA/EGF, BLOOD COAGULATION, 2 PLASMA, SERINE PROTEASE, CALCIUMBINDING, HYDROLASE, 3 GLYCOPROTEIN	SERINE PROTEASE FVIIA; FVIIA; BLOOD COAGULATION, SERINE PROTEASE	SERINE PROTEASE FVIIA; FVIIA; BLOOD COAGULATION, SERINE PROTEASE	SERINE PROTEASE FVIIA; FVIIA; BLOOD COAGULATION, SERINE PROTEASE
Coumpound	PRO-ARG; CHAIN: I;	COAGULATION FACTOR VIIA (LIGHT CHAIN); CHAIN: L; COAGULATION FACTOR VIIA (HEAVY CHAIN); CHAIN: H; TRIPEPTIDYL INHIBITOR; CHAIN: C;	COAGULATION FACTOR VIIA (LIGHT CHAIN); CHAIN: L; COAGULATION FACTOR VIIA (HEAVY CHAIN); CHAIN: H; TRIPEPTIDYL INHIBITOR; CHAIN: C;	COAGULATION FACTOR VIIA (LIGHT CHAIN); CHAIN: L; COAGULATION FACTOR VIIA (HEAVY CHAIN);
SeqFold Score				
PMF		-0.19	-0.18	-0.18
Verify Score		0.16	0.32	0.31
PSI- BLAST		5.1e-11	5.1e-13	6.8e-10
End		1339	427	868
Start AA		1263	334	822
Chain ID		L	7	1
PDB ID	,	1qfk	1qfk	1qfk
SEQ NO:		129	129	129

	····	_ 					
PDB annotation		MEMBRANE ADHESION SHORT CONSENSUS REPEAT, SUSHI, COMPLEMENT CONTROL PROTEIN, 2 N-GLYCOSYLATION, MULTI- DOMAIN, MEMBRANE ADHESION	BLOOD COAGULATION FACTOR STUART FACTOR; BLOOD COAGULATION FACTOR, SERINE PROTEINASE, EPIDERMAL 2 GROWTH FACTOR LIKE DOMAIN	BLOOD COAGULATION FACTOR STUART FACTOR; BLOOD COAGULATION FACTOR, SERINE PROTEINASE, EPIDERMAL 2 GROWTH FACTOR LIKE DOMAIN	BLOOD COAGULATION FACTOR STUART FACTOR; BLOOD COAGULATION FACTOR, SERINE PROTEINASE, EPIDERMAL 2 GROWTH FACTOR LIKE DOMAIN		
Coumpound	CHAIN: H; TRIPEPTIDYL INHIBITOR; CHAIN: C;	HUMAN BETA2- GLYCOPROTEIN I; CHAIN: A;	BLOOD COAGULATION FACTOR XA; CHAIN: L, C;	BLOOD COAGULATION FACTOR XA; CHAIN: L, C;	BLOOD COAGULATION FACTOR XA; CHAIN: L, C;	LECTIN (AGGLUTININ) WHEAT GERM AGGLUTININ (ISOLECTIN 2) 9WGA 3	LECTIN (AGGLUTININ) WHEAT GERM AGGLUTININ
SeqFold Score							
PMF Score		-0.15	-0.07	-0.13	-0.19	-0.19	-0.19
Verify Score		0.20	0.22	0.22	0.11	0.02	0.02
PSI- BLAST		3.9e-08	3.4e-10	1e-10	3.4e-09	5.1e-11	5.1e-11
End AA		488	427	868	940	1364	1364
Start AA		379	334	822	855	1219	1219
Chain ID		A	J	Г	ı	∢ .	V
PDB ID		1qub	lxka	1xka	lxka	9wga	9wga
SEQ NO:		129	129	129	129	129	129

PDB annotation		·	·				
Coumpound	(ISOLECTIN 2) 9WGA 3	LECTIN (AGGLUTININ) WHEAT GERM AGGLUTININ (ISOLECTIN 2) 9WGA 3	LECTIN (AGGLUTININ)				
SeqFold Score							
PMF Score		-0.19	-0.19	-0.18	-0.18	-0.17	-0.17
Verify Score		0.08	0.08	0.31	0.31	0.13	0.13
PSI- BLAST		5.1e-14	5.1e-14	1.5e-11	1.5e-11	3.46-12	3.4e-12
End AA		420	420	544	544	907	200
Start AA		27.7	772	318	318	757	757
Chain ID		A	A	₩	∢	⋖	A
PDB ID		9wga	9wga	9wga	9wga	9wga	9wga
SEQ NO:		129	129	129	129	129	129

PDB annotation				
Coumpound	WHEAT GERM AGGLUTININ (ISOLECTIN 2) 9WGA 3	LECTIN (AGGLUTININ) WHEAT GERM AGGLUTININ (ISOLECTIN 2) 9WGA 3	LECTIN (AGGLUTININ) WHEAT GERM AGGLUTININ (ISOLECTIN 2) 9WGA 3	COAGULATION FACTOR EGF-LIKE MODULE OF BLOOD COAGULATION FACTOR X (N- TERMINAL, 1APO 3 APO FORM) (NMR, 13 STRUCTURES) 1APO 4 COAGULATION FACTOR EGF-LIKE MODULE OF BLOOD COAGULATION FACTOR X (N- TERMINAL, 1APO 3 APO FORM) (NMR, 13 STRUCTURES) 11 STRUCTURES)
SeqFold Score				
PMF Score		-0.12	-0.12	0.53
Verify Score	_	0.29	0.29	0.37
PSI- BLAST		5.1e-13	5.1e-13	1.3e-06
End AA		975	975	1245
Start AA		777	777	1210
Chain ID		V	¥	
PDB ID		9wga	9wga	1аро 1аро
ğ a ş		129	129	130

PDB annotation	GLYCOSIDASE CGTASE; 1CIU 8 THERMOSTABLE 1CIU 14						
Coumpound	CYCLODEXTRIN GLYCOSYLTRANSF ERASE; 1CTU 6 CHAIN: NULL; 1CTU	CYCLODEXTRIN GLYCOSYLTRANSF ERASE; 1CIU 6 CHAIN: NULL; 1CIU	CYCLODEXTRIN GLYCOSYLTRANSF ERASE; 1CIU 6 CHAIN: NULL; 1CIU	CYCLODEXTRIN GLYCOSYLTRANSF ERASE; ICIU 6 CHAIN: NULL; ICIU	CYCLODEXTRIN GLYCOSYLTRANSF ERASE; ICIU 6 CHAIN: NULL; ICIU	CYCLODEXTRIN GLYCOSYLTRANSF ERASE; 1CIU 6 CHAIN: NULL; 1CIU	CYCLODEXTRIN GLYCOSYLTRANSF ERASE; 1CTU 6 CHAIN: NULL; 1CTU
SeqFold Score	·						
PMF Score	-0.19	-0.19	-0.18	-0.18	-0.19	-0.19	-0.15
Verify Score	0.05	0.05	0.01	0.01	0.05	0.05	0.03
PSI- BLAST	5.2e-34	5.2e-34	1.3e-32	1.3e-32	1.3e-26	1.3e-26	3.9e-22
End	385	385	783	783	1044	1044	1177
Start AA	39	39	404	404	699	699	863
Chain ID							
PDB ID	1ciu	lciu	1ciu	lciu	1ciu	1ciu	1ciu
SEQ B G SE	130	130	130	130	130	130	130

PDB annotation		GLYCOSIDASE CGTASE; 1CIU 8 THERMOSTABLE 1CIU 14	STRUCTURAL PROTEIN INTEGRIN- BINDING PROTEIN, INV GENE	BLOOD COAGULATION, SERINE	2 RECEPTOR ENZYME, INHIBITOR,	PROTEASE/COFACTOR/LIGAND)				BLOOD COAGULATION, SERINE	PROTEASE, COMPLEX, CO-FACTOR,	GLA, EGF, 3 COMPLEX (SERINE	PROTEASE/COFACTOR/LIGAND)					
Coumpound	7	CYCLODEXTRIN GLYCOSYLTRANSF ERASE; 1CIU 6 CHAIN: NULL; 1CIU	INVASIN; CHAIN: A;	BLOOD COAGIII ATION	FACTOR VIIA;	SOLUBLE TISSUE	FACTOR; CHAIN: T,	CHLOROMETHYLKE	TONE (DFFRCMK) WITH CHAIN: C;	ВГООД	COAGULATION FACTOR VITA:	CHAIN: L, H;	SOLUBLE TISSUE FACTOR; CHAIN: T,					
SeqFold Score					101.45	101.45												
PMF Score		-0.15	-0.20	-0.20			-0.19	-0.19	0.04						0.04			
Verify Score		0.03	0.05	0.05			0.04	0.04	0.15						0.15			
PSI- BLAST		3.9e-22	9.1e-60	9.1e-60	1.2e-61	1.2e-61	1e-56	1e-56	8.5e-10		-				8.5e-10			
End AA		1177	749	749	966	966	1082	1082	1282						1282			
Start AA		863	264	264	521	521	561	561	1210						1210			
Chain ID			¥	A	Ą	A	V	V	T						I			
PDB CD		lciu	Icwv	Icwv	lcwv	lcwv	lcwv	lcwv	1dan					•	1dan			-
SEQ NO:		130	130	130	130	130	130	130	130						130			

PDB annotation		COAGULATION FACTOR CRYSTAL STRUCTURE, EPIDERMAL GROWTH FACTOR, EGF, 2 CALCTUM- BINDING, EGF-LIKE DOMAIN, STRUCTURE AND FUNCTION, 3 HUMAN FACTOR IX, COAGULATION FACTOR	COAGULATION FACTOR CRYSTAL STRUCTURE, EPIDERMAL GROWTH FACTOR, EGF, 2 CALCIUM- BINDING, EGF-LIKE DOMAIN, STRUCTURE AND FUNCTION, 3 HUMAN FACTOR IX, COAGULATION FACTOR	BLOOD CLOTTING COMPLEX(SERINE PROTEASE/COFACTOR/LIGAND), BLOOD COAGULATION, 2 SERINE PROTEASE, COMPLEX, CO-FACTOR, RECEPTOR ENZYME, 3 INHIBITOR, GLA, EGF, COMPLEX (SERINE 4 PROTEASE/COFACTOR/LIGAND), BLOOD CLOTTING	BLOOD CLOTTING COMPLEX(SERINE PROTEASE/COFACTOR/LIGAND), BLOOD COAGULATION, 2 SERINE PROTEASE, COMPLEX, CO-FACTOR, RECEPTOR ENZYME, 3 INHIBITOR, GLA, EGF, COMPLEX (SERINE 4
Coumpound	U; D-PHE-PHE-ARG- CHLOROMETHYLKE TONE (DFFRCMK) WITH CHAIN: C;	FACTOR IX; CHAIN: B, C;	FACTOR IX; CHAIN: B, C;	BLOOD COAGULATION FACTOR VIIA; CHAIN: L; BLOOD COAGULATION FACTOR VIIA; CHAIN: H; SOLUBLE TISSUE FACTOR; CHAIN: T; 5L15; CHAIN: I;	BLOOD COAGULATION FACTOR VIIA; CHAIN: L; BLOOD COAGULATION FACTOR VIIA; CHAIN: H; SOLUBLE
SeqFold Score					
PMF Score		0.76	0.76	0.00	0.00
Verify Score		0.32	0.32	-0.03	-0.03
PSI- BLAST		5.1e-07	5.1e-07	8.5e-10	8.5e-10
End		1242	1242	1282	1282
Start AA		1210	1210	1210	1210
Chain ID		В	B.	. 1	1
PDB ID		ledm	1edm	lfak	lfak
SEQ NO EQ		130	130	130	130

PDB annotation	PROTEASE/COFACTOR/LIGAND), BLOOD CLOTTING	COMPLEX (BLOOD COAGULATION/INHIBITOR) CHRISTMAS FACTOR; COMPLEX, INHIBITOR, HEMOPHILIA/EGF, BLOOD COAGULATION, 2 PLASMA, SERINE PROTEASE, CALCIUM- BINDING, HYDROLASE, 3 GLYCOPROTEIN	COMPLEX (BLOOD COAGULATION/INHIBITOR) CHRISTMAS FACTOR; COMPLEX, INHIBITOR, HEMOPHILIA/EGF, BLOOD COAGULATION, 2 PLASMA, SERINE PROTEASE, CALCIUM- BINDING, HYDROLASE, 3 GLYCOPROTEIN	COMPLEX (BLOOD COAGULATION/INHIBITOR) CHRISTMAS FACTOR; COMPLEX, INHIBITOR, HEMOPHILIA/EGF, BLOOD COAGULATION, 2 PLASMA, SERINE PROTEASE, CALCIUM- BINDING, HYDROLASE, 3 GLYCOPROTEIN	COMPLEX (BLOOD COAGULATION/INHIBITOR) CHRISTMAS FACTOR; COMPLEX, INHIBITOR, HEMOPHILIA/BGF, BLOOD COAGULATION, 2 PLASMA, SERINE PROTBASE, CALCIUM- BINDING, HYDROLASE, 3 GLYCOPROTEIN
Coumpound	TISSUE FACTOR; CHAIN: T; 5L15; CHAIN: I;	FACTOR IXA; CHAIN: C, L,; D-PHE- PRO-ARG; CHAIN: I;	FACTOR IXA; CHAIN: C, L,; D-PHB- PRO-ARG; CHAIN: I;	FACTOR IXA; CHAIN: C, L,; D-PHB- PRO-ARG; CHAIN: I;	FACTOR IXA; CHAIN: C, L,; D-PHE- PRO-ARG; CHAIN: 1;
SeqFold Score					
PMF Score		-0.11	-0.11	0.11	0.11
Verify Score		0.04	0.04	0.15	0.15
PSI- BLAST		5.2e-10	5.2e-10	16-08	1e-08
End		1242	1242	1273	1273
Start		1189	1189	1210	1210
Chain ID		L)	_L	ļ.i	ъ
PDB TD		1pfx	lpfx	lpfx	1pfx
S e S		130	130	130	130

PDB annotation	SERINE PROTEASE FVIIA; FVIIA; BLOOD COAGULATION, SERINE PROTEASE	SERINE PROTEASE FVIIA; FVIIA; BLOOD COAGULATION, SERINE PROTEASE	PLASMINOGEN ACTIVATION	PLASMINOGEN ACTIVATION	PLASMINOGEN ACTIVATION	PLASMINOGEN ACTIVATION
Coumpound	COAGULATION FACTOR VIIA (LIGHT CHAIN); CHAIN: L; COAGULATION FACTOR VIIA (HEAVY CHAIN); CHAIN: H; TRIPEPTIDYL INHIBITOR; CHAIN: C;	COAGULATION FACTOR VIIA (LIGHT CHAIN); CHAIN: L; COAGULATION FACTOR VIIA (HEAVY CHAIN); CHAIN: H; TRIPEPTIDYL INHIBITOR; CHAIN: C;	T-PLASMINOGEN ACTIVATOR F1-G; ITPG 7 CHAIN: NULL; ITPG 8	T-PLASMINOGEN ACTIVATOR F1-G; 1TPG 7 CHAIN: NULL; 1TPG 8	T-PLASMINOGEN ACTIVATOR F1-G; ITPG 7 CHAIN: NULL; 1TPG 8	T-PLASMINOGEN
SeqFold Score						
PMF Score	-0.13	-0.13	0.07	0.07	0.03	0.03
Verify Score	0.04	90.04	0.44	0.44	-0.12	-0.12
PSI- BLAST	3.4e-09	3.4e-09	2.6e-10	2.6e-10	1.7e-07	1.7e-07
End	1282	1282	1242	1242	1246	1246
Start	1214	1214	1189	1189	1197	1197
Chain	1	ı				
PDB ID	1qfk	1qfk	1tpg	14рд	1tpg	1tpg
SEQ No B	130	130	130	130	130	130

PDB annotation		GLYCOPROTEIN GLYCOPROTEIN, HYDROLASE, SERINE PROTEASE, PLASMA, BLOOD 2 COAGULATION FACTOR	GLYCOPROTEIN GLYCOPROTEIN, HYDROLASE, SERINE PROTEASE, PLASMA, BLOOD 2 COAGULATION FACTOR			SUGAR BINDING PROTEIN C-TYPE LECTIN, CRD, SP-D, COLECTIN, ALPHA-HELICAL COILED- 2 COIL, LUNG SURFACTANT, SUGAR BINDING PROTEIN	SIGNALING PROTEIN HEPATIC LECTIN H1; C-TYPE LECTIN CRD	COMPLEX (BLOOD
Coumpound	ACTIVATOR F1-G; 1TPG 7 CHAIN: NULL; 1TPG 8	COAGULATION FACTOR X; CHAIN: NULL;	COAGULATION FACTOR X; CHAIN: NULL;	LECTIN (AGGLUTININ) WHEAT GERM AGGLUTININ (ISOLECTIN 2) 9WGA 3	LECTIN (AGGLUTININ) WHEAT GERM AGGLUTININ (ISOLECTIN 2) 9WGA 3	LUNG SURFACTANT PROTEIN D; CHAIN: A, B, C;	ASIALOGLYCOPROT EIN RECEPTOR 1; CHAIN: A;	ACTIVATED
SeqFold Score								
PMF Score		-0.14	-0.14	-0.19	-0.19	0.89	1.00	0.03
Verify Score		0.29	0.29	0.22	0.22	0.45	1.03	-0.03
PSI- BLAST		3.9e-10	3.9e-10	5.1e-08	5.1e-08	6.5e-42	le-39	le-11
End		1245	1245	1293	1293	308	311	374
Start		1189	1189	1191	1191	153	184	292
Chain U				<	<	V .	A	1
PDB CD		1whe	lwhe	9wga	9wga	1508	ldv8	laut
SEQ	Ö	130	130	130	130	131	131	132

PDB annotation	COAGULATION/INHIBITOR) AUTOPROTHROMBIN IIA; HYDROLASE, SERINE PROTEINASE), PLASMA CALCIUM BINDING, 2 GLYCOPROTEIN, COMPLEX (BLOOD COAGULATION/INHIBITOR)	GLYCOPROTEIN MEMBRANE COFACTOR PROTEIN (MCP); VIRUS RECEPTOR, COMPLEMENT COFACTOR, SHORT CONSENSUS REPEAT, 2 SCR, MEASLES VIRUS, GLYCOPROTEIN	GLYCOPROTEIN MEMBRANE COFACTOR PROTEIN (MCP); VIRUS RECEPTOR, COMPLEMENT COFACTOR, SHORT CONSENSUS REPEAT, 2 SCR, MEASLES VIRUS, GLYCOPROTEIN	GLYCOPROTEIN MEMBRANE COFACTOR PROTEIN (MCP); VIRUS RECEPTOR, COMPLEMENT COFACTOR, SHORT CONSENSUS REPEAT, 2 SCR, MEASLES VIRUS, GLYCOPROTEIN	GLYCOPROTEIN MEMBRANE COFACTOR PROTEIN (MCP); VIRUS RECEPTOR, COMPLEMENT COFACTOR, SHORT CONSENSUS REPEAT, 2 SCR, MEASLES VIRUS, GLYCOPROTEIN	GLYCOPROTEIN MEMBRANE COFACTOR PROTEIN (MCP); VIRUS RECEPTOR, COMPLEMENT COFACTOR, SHORT CONSENSUS
Coumpound	PROTEIN C; CHAIN: C, L; D-PHE-PRO- MAI; CHAIN: P;	C, D, E, F;	CD46; CHAIN: A, B,	CD46; CHAIN: A, B, C, D, E, F;	C, D, B, F,	CD46; CHAIN: A, B, C, D, B, F;
SeqFold Score						
PMF Score		1.00	1.00	1.00	66:0	0.23
Verify Score		0.71	0.10	0.62	0.53	-0.18
PSI- BLAST		2.6e-16	6.5e-20	1.3e-25	5.1e-12	1.4e-09
End AA		267	330	387	388	08
Start AA		155	213	272	284	2
Chain ID	•	A	A	¥	¥	A
PDB TD		1ckl	1cki	1cki	1ckl	1ckl
SEQ B B S		132	132	132	132	132

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РDВ аппоtation	REPEAT, 2 SCR, MEASLES VIRUS, GLYCOPROTEIN	GLYCOPROTEIN MEMBRANE COFACTOR PROTEIN (MCP); VIRUS RECEPTOR, COMPLEMENT COFACTOR, SHORT CONSENSUS REPEAT, 2 SCR, MEASLES VIRUS, GLYCOPROTEIN	GLYCOPROTEIN MEMBRANE COFACTOR PROTEIN (MCP); VIRUS RECEPTOR, COMPLEMENT COFACTOR, SHORT CONSENSUS REPEAT, 2 SCR, MEASLES VIRUS, GLYCOPROTEIN	GLYCOPROTEIN MEMBRANE COFACTOR PROTEIN (MCP); VIRUS RECEPTOR, COMPLEMENT COFACTOR, SHORT CONSENSUS REPEAT, 2 SCR, MEASLES VIRUS, GLYCOPROTEIN	GLYCOPROTEIN MEMBRANE COFACTOR PROTEIN (MCP); VIRUS RECEPTOR, COMPLEMENT COFACTOR, SHORT CONSENSUS REPEAT, 2 SCR, MEASLES VIRUS, GLYCOPROTEIN	GLYCOPROTEIN MEMBRANE COFACTOR PROTEIN (MCP); VIRUS RECEPTOR, COMPLEMENT COFACTOR, SHORT CONSENSUS REPEAT, 2 SCR, MEASLES VIRUS, GLYCOPROTEIN	GLYCOPROTEIN MEMBRANE COFACTOR PROTEIN (MCP); VIRUS
Coumpound		CD46; CHAIN: A, B,	C, D, E, F,	C, D, E, F;	CD46; CHAIN: A, B, C, D, E, F;	C, D, E, F;	CD46; CHAIN: A, B, C, D, E, F;
SeqFold Score				(
PMF		66.0	1.00	66.0	0.99	0.77	99.0
Verify Score		0.86	0.40	0.43	0.20	0.63	0.38
PSI- BLAST		9.1e-28	7.8e-23	5.2e-20	2.6e-21	6.5e-22	5.1e-10
End		445	505	145	562	93	211
Start		332	390	40	448	4	26
Chain ID		∢	4	4	4	∢	A
PDB ID		10/2	1cki	1cki	1ckl	1cki	1ckl
ğa ş		132	132	132	132	132	132

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PDB annotation	RECEPTOR, COMPLEMENT COFACTOR, SHORT CONSENSUS REPEAT, 2 SCR, MEASLES VIRUS, GLYCOPROTEIN	COMPLEMENT INHIBITOR VCP, SP35; COMPLEMENT, NMR, MODULES, PROTEIN STRUCTURE, VACCINIA VIRUS	COMPLEMENT INHIBITOR VCP, SP35; COMPLEMENT, NMR, MODULES, PROTEIN STRUCTURE, VACCINIA VIRUS	COMPLEMENT INHIBITOR VCP, SP35; COMPLEMENT, NMR, MODULES, PROTEIN STRUCTURE, VACCINIA VIRUS	COMPLEMENT INHIBITOR VCP, SP35; COMPLEMENT, NMR, MODULES, PROTEIN STRUCTURE, VACCINIA VIRIS	COMPLEMENT INHIBITOR VCP, SP35, COMPLEMENT, NMR, MODULES, PROTEIN STRUCTURE, VACCINIA VIRUS	COMPLEMENT INHIBITOR VCP, SP35; COMPLEMENT, NMR, MODULES, PROTEIN STRUCTURE, VACCINIA VIRUS	COMPLEMENT INHIBITOR VCP, SP35; COMPLEMENT, NMR, MODULES, PROTEIN STRUCTURE, VACCINIA VIRIIS	COMPLEMENT INHIBITOR VCP, SP35; COMPLEMENT, NMR,
Coumpound		COMPLEMENT CONTROL PROTEIN; CHAIN: A;	COMPLEMENT CONTROL PROTEIN;						
SeqFold Score									
PMF Score		1.00	0.98	0.51	1.00	1.00	1.00	1.00	0.99
Verify Score		0.71	0.48	0.53	0.75	0.82	0.75	0.19	-0.08
PSI- BLAST		3.9e- <u>2</u> 1	8.5e-18	5.2e-18	7.8e-27	6.5e-31	1.4e-16	1.7e-17	8.5e-10
End AA		260	266	321	386	44	443	501	08
Start AA		154	154	212	270	331	332	388	3
Chain 19		A	A	Ą	A	A	A	Ą	A
PDB TD		1e5g	1e5g	le5g	le5g	1e5g	1e5g	1e5g	le5g
S e S		132	132	132	132	132	132	132	132

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PDB annotation	MODULES, PROTEIN STRUCTURE, VACCINIA VIRUS	COMPLEMENT INHIBITOR VCP, SP35; COMPLEMENT, NMR, MODULES, PROTEIN STRUCTURE, VACCINIA VIRUS	COMPLEMENT INHIBITOR VCP, SP35; COMPLEMENT, NMR, MODULES, PROTEIN STRUCTURE, VACCINIA VIRUS	COMPLEMENT INHIBITOR VCP, SP35; COMPLEMENT, NMR, MODULES, PROTEIN STRUCTURE, VACCINIA VIRUS	COMPLEMENT INHIBITOR VCP, SP35; COMPLEMENT, NMR, MODULES, PROTEIN STRUCTURE, VACCINIA VIRUS	COMPLEMENT INHIBITOR VCP, SP35, COMPLEMENT, NMR, MODULES, PROTEIN STRUCTURE, VACCINIA VIRUS	COMPLEMENT INHIBITOR VCP, SP35, COMPLEMENT, NMR, MODULES, PROTEIN STRUCTURE, VACCINIA VIRUS	COMPLEMENT INHIBITOR VCP, SP35, COMPLEMENT, NMR, MODULES, PROTEIN STRUCTURE, VACCINIA VIRUS	COMPLEMENT INHIBITOR VCP, SP35; COMPLEMENT, NMR, MODULES, PROTEIN STRUCTURE, VACCINIA VIRUS
Coumpound	CHAIN: A;	COMPLEMENT CONTROL PROTEIN; CHAIN: A;	COMPLEMENT CONTROL PROTEIN; CHAIN: A;	COMPLEMENT CONTROL PROTEIN; CHAIN: A;	COMPLEMENT CONTROL PROTEIN; CHAIN: A;	COMPLEMENT CONTROL PROTEIN; CHAIN: A;	COMPLEMENT CONTROL PROTEIN; CHAIN: A;	COMPLEMENT CONTROL PROTEIN; CHAIN: A;	COMPLEMENT CONTROL PROTEIN; CHAIN: A;
SeqFold Score									
PMF		66.0	0.72	0.93	1.00	1.00	0.42	1.00	0.75
Verify Score		0.63	0.70	0.15	0.26	0.46	9.68	0.53	0.54
PSI- BLAST		9.1e-24	3.4e-11	1.2e-14	1.3e-26	1.2e-23	2.6e-12	6.5e-20	3.4e-15
End		145	151	960	560	83	999	209	210
Start		40	40	448	448	4	506	97	97
Chain TD		V	A	V	A	A	¥	4	¥
PDB CD		le5g	1e5g	le5g	le5g	le5g	1e5g	1e5g	1e5g
S A S		132	132	132	132	132	132	132	132

PDB annotation	MATRIX PROTEIN EXTRACELLULAR MATRIX, CALCIUM-BINDING, GLYCOPROTEIN, 2 REPEAT, SIGNAL, MULTIGENE FAMILY, DISEASE MUTATION, 3 EGF-LIKE DOMAIN, HUMAN FIBRILLIN-1 FRAGMENT, MATRIX PROTEIN	MATRIX PROTEIN EXTRACELLULAR MATRIX, CALCIUM-BINDING, GLYCOPROTEIN, 2 REPEAT, SIGNAL, MULTIGENE FAMILY, DISEASE MUTATION, 3 BGF-LIKE DOMAIN, HUMAN FIBRILLIN-1 FRAGMENT, MATRIX PROTEIN	LIPID BINDING PROTEIN LDL RECEPTOR; BETA HAIRPIN, 3-10 HELIX, CALCIUM BINDING			
Coumpound	FIBRILLIN; CHAIN: NULL;	FIBRILLIN; CHAIN: NULL;	LOW-DENSITY LIPOPROTEIN RECEPTOR; CHAIN: A;	GLYCOPROTEIN 16TH COMPLEMENT CONTROL PROTEIN (/CCP\$) OF FACTOR H 1HCC 3	GLYCOPROTEIN 16TH COMPLEMENT CONTROL PROTEIN (/CCP\$) OF FACTOR H 1HCC 3	GLYCOPROTEIN 16TH COMPLEMENT CONTROL PROTEIN (/CCP\$) OF FACTOR H 1HCC 3
SeqFold Score						
PMF Score	-0.19	0.04	-0.17	0.47	0.46	0.70
Verify Score	0.18	-0.23	0.37	-0.09	0.16	0.71
PSI- BLAST	5.1e-12	6.8e-12	1e-10	5.2e-09	6.5e-13	3.9e-12
End	370	285	452	208	385	94
Start AA	289	503	376	154	330	38
Chain ID			¥			
aga eg	lemn	lemn	1f5y	lhcc	Ihcc	1hcc
SEQ NO:	132	132	132	132	132	132

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Coumpound	GLYCOPROTEIN 16TH COMPLEMENT CONTROL PROTEIN (/CCP\$) OF FACTOR H 1HCC 3	GLYCOPROTEIN 16TH COMPLEMENT CONTROL PROTEIN (/CCP\$) OF FACTOR H 1HCC 3	GLYCOPROTEIN FACTOR H, 15TH AND 16TH C. MODULE PAIR (NMR, MINIMIZED 1HFHA 1 AVERAGED STRUCTURE) 1HFH 4 1HFHA 5	GLYCOPROTEIN FACTOR H, 15TH AND 16TH C. MODULE PAIR (NMR, MINIMIZED 1HFHA 1 AVERAGED STRUCTURE) 1HFH 4 1HFHA 5	GLYCOPROTEIN FACTOR H, 15TH AND 16TH C- MODULE PAIR (NMR, MINIMIZED 1HFHA 1
SeqFold Score				83.97	
PMF Score	0.01	0.13	0.31		0.76
Verify Score	-0.64	0.10	0.47		0.30
PSI- BLAST	1.2e-07	2.6e-15	5.1e-12	3.4e-11	6.8e-12
End AA	35	559	267	444	559
Start	4	503	151	328	4 4 44
Chain ID					
PDB ED	1hcc	lhcc	1hfh	1hfh	# <u>#</u>
S a S	132	132	132	132	132

PDB annotation															
Coumpound	STRUCTURE) 1HFH 4 1HFHA 5	GLYCOPROTEIN FACTOR H, 15TH AND 16TH C- MODULE PAIR	(NMAK, MINIMIZED 1HFHA 1 AVERAGED STRUCTURE) 1HFH 4 1HFHA 5	GLYCOPROTEIN FACTOR H, 15TH C- MODULE PAIR	(NMR, MINIMIZED AVERAGED 1HFIA 1 STRUCTURE) 1HFI 4	GLYCOPROTEIN	FACTOR H, 15TH C- MODULE PAIR	(NMR, MINIMIZED	STRUCTURE) 1HFI 4 1HFIA 5	GLYCOPROTEIN FACTOR H. 15TH C-	MODULE PAIR	(NMR, MINIMIZED AVERAGED 1HFIA 1	STRUCTURE) 1HFI 4	1HFIA 5	GLYCOPROTEIN FACTOR H, 15TH C- MODULE PAIR
SeqFold Score				·											
PMF Score	,	0.75		0.95		96.0				9.08					0.18
Verify Score		0.32		0.55		0.74				0.87					0.24
PSI- BLAST		1e-09		1.3e-10		1.3e-13		- 1.7	-	6.5e-12					1e-07
End		208		209		386	}			83					36
Start AA		26		154	<u>-</u>	330	}			38					4
Chain ID							-								
PDB CD		Than		1111		1hfi				1hfi					1146
SEQ NO:		132	,	132		132				132					132

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PDB annotation		·	GLYCOPROTEIN GLYCOPROTEIN	MEMBRANE ADHESION SHORT CONSENSUS REPEAT, SUSHI, COMPLEMENT CONTROL PROTEIN, 2 N-GLYCOSYLATION, MULTI- DOMAIN, MEMBRANE ADHESION	MEMBRANE ADHESION SHORT CONSENSUS REPEAT, SUSHI, COMPLEMENT CONTROL PROTEIN, 2 N-GLYCOSYLATION, MULTI- DOMAIN, MEMBRANE ADHESION	MEMBRANE ADHESION SHORT CONSENSUS REPEAT, SUSHI, COMPLEMENT CONTROL PROTEIN, 2 N-GLYCOSYLATION, MULTI- DOMAIN, MEMBRANE ADHESION	MEMBRANE ADHESION SHORT CONSENSUS REPEAT, SUSHI, COMPLEMENT CONTROL PROTEIN, 2 N-GLYCOSYLATION, MULTI- DOMAIN, MEMBRANE ADHESION	MEMBRANE ADHESION SHORT
Coumpound	(NMR, MINIMIZED AVERAGED 1HFIA 1 STRUCTURE) 1HFI 4 1HFIA 5	GLYCOPROTEIN FACTOR H, 15TH C- MODULE PAIR (NMR, MINIMIZED AVERAGED 1HFIA 1 STRUCTURE) 1HF1 4 1HFIA 5	LAMININ; CHAIN: NULL;	HUMAN BETA2- GLYCOPROTEIN I; CHAIN: A;	HUMAN BETA2- GLYCOPROTBIN I; CHAIN: A;	HUMAN BETA2- GLYCOPROTEIN I; CHAIN: A;	HUMAN BETA2- GLYCOPROTEIN I; CHAIN: A;	HUMAN BETA2-
SeqFold Score					189.59			
PMF Score		0.59	-0.18	96:0		1.00	1.00	98.0
Verify Score		0.24	0.00	0.29		0.41	0.37	90.0
PSI- BLAST		le-16	le-13	1.7e-28	6.5e-39	6.8e-28	1e-31	1.7e-35
End AA		559	426	329	522	489	503	270
Start AA		503	275	11	210	212	288	2
Chain TO				¥	⋖ .	V	«	¥
EDB CO		1hfi	1klo	1qub	lqub	1qub	lqub	1qub
රි _ස දූ		132	132	132	132	132	132	132

PDB annotation	CONSENSUS REPEAT, SUSHI, COMPLEMENT CONTROL PROTEIN, 2 N-GLYCOSYLATION, MULTI- DOMAIN, MEMBRANE ADHESION	MEMBRANE ADHESION SHORT CONSENSUS REPEAT, SUSHI, COMPLEMENT CONTROL PROTEIN, 2 N-GLYCOSYLATION, MULTI- DOMAIN, MEMBRANE ADHESION	MEMBRANE ADHESION SHORT CONSENSUS REPEAT, SUSHI, COMPLEMENT CONTROL PROTEIN, 2 N-GLYCOSYLATION, MULTI- DOMAIN, MEMBRANE ADHESION	COMPLEMENT INHIBITOR SP35, VCP, VACCINIA VIRUS SP35, COMPLEMENT INHIBITOR, COMPLEMENT MODULE, SCR, SUSHI DOMAIN, 2 MODULE PAIR	COMPLEMENT INHIBITOR SP35, VCP, VACCINIA VIRUS SP35; COMPLEMENT INHIBITOR, COMPLEMENT MODULE, SCR, SUSHI DOMAIN, 2 MODULE PAIR	COMPLEMENT INHIBITOR SP35, VCP, VACCINIA VIRUS SP35, COMPLEMENT INHIBITOR, COMPLEMENT MODULE, SCR, SUSHI DOMAIN, 2 MODULE PAIR	COMPLEMENT INHIBITOR SP35, VCP, VACCINIA VIRUS SP35; COMPLEMENT INHIBITOR, COMPLEMENT MODULE, SCR, SUSHI DOMAIN, 2 MODULE PAIR
Coumpound	GLYCOPROTEIN I; CHAIN: A;	HUMAN BETA2- GLYCOPROTEIN I; CHAIN: A;	HUMAN BETA2- GLYCOPROTEIN I; CHAIN: A;	VACCINIA VIRUS COMPLEMENT CONTROL PROTEIN; CHAIN: NULL;			
SeqFold Score							
PMF Score		1.00	1.00	1.00	0.75	0.34	0.92
Verify Score		0.53	0.30	0.48	0.28	0.44	0.53
PSI- BLAST		1.7e-41	6.8e-22	1.7e-14	5.1e-14	1.7e-12	5.1e-17
End		576	589	267	327	385	4 4 44
Start AA		331	388	153	211	271	330
Chain ID		Ą	A				
PDB ID		1qub	1qub	lvvc	lvvc	lvvc	Ivvc
SEQ NO:		132	132	132	132	132	132

PDB annotation	COMPLEMENT INHIBITOR SP35, VCP, VACCINIA VIRUS SP35; COMPLEMENT INHIBITOR, COMPLEMENT MODULE, SCR, SUSHI DOMAIN, 2 MODULE PAIR	COMPLEMENT INHIBITOR SP35, VCP, VACCINIA VIRUS SP35; COMPLEMENT INHIBITOR, COMPLEMENT MODULE, SCR, SUSHI DOMAIN, 2 MODULE PAIR	COMPLEMENT INHIBITOR SP35, VCP, VACCINIA VIRUS SP35; COMPLEMENT INHIBITOR, COMPLEMENT MODULE, SCR, SUSHI DOMAIN, 2 MODULE PAIR	COMPLEMENT INHIBITOR SP35, VCP, VACCINIA VIRUS SP35, COMPLEMENT INHIBITOR, COMPLEMENT MODULE, SCR, SUSHI DOMAIN, 2 MODULE PAIR	COMPLEMENT INHIBITOR SP35, VCP, VACCINIA VIRUS SP35; COMPLEMENT INHIBITOR, COMPLEMENT MODULE, SCR, SUSHI DOMAIN, 2 MODULE PAIR	COMPLEMENT INHIBITOR SP35, VCP., VACCINIA VIRUS SP35; COMPLEMENT INHIBITOR, COMPLEMENT MODULE, SCR, SUSHI DOMAIN, 2 MODULE PAIR	BLOOD COAGULATION FACTOR STUART FACTOR; BLOOD COAGULATION FACTOR, SERINE PROTEINASE, EPIDERMAL 2
Coumpound	VACCINIA VIRUS COMPLEMENT CONTROL PROTEIN; CHAIN: NULL;	VACCINIA VIRUS COMPLEMENT CONTROL PROTEIN; CHAIN: NULL;	VACCINIA VIRUS COMPLEMENT CONTROL PROTEIN; CHAIN: NULL;	VACCINIA VIRUS COMPLEMENT CONTROL PROTEIN; CHAIN: NULL;	VACCINIA VIRUS COMPLEMENT CONTROL PROTEIN; CHAIN: NULL;	VACCINIA VIRUS COMPLEMENT CONTROL PROTEIN; CHAIN: NULL;	BLOOD COAGULATION FACTOR XA; CHAIN: L, C;
SeqFold Score		91.84					
PMF Score	1.00		0.35	0.18	0.01	0.82	-0.17
Verify Score	0.33	_	-0.10	0.02	-0.14	0.40	0.17
PSI- BLAST	5.1e-15	5.2e-21	6.8e-14	2.6e-15	1.7e-10	3.4e-14	3.4e-09
End AA	502	504	559	584	589	208	260
Start	388	388	446	505	505	97	180
Chain ID							ı
PDB ID	·lvvc	lwc	lvvc	1wc	lvvc	1wc	1xka
SEQ No de		132	132	132	132	132	132

PDB annotation	GROWTH FACTOR LIKE DOMAIN			OXIDOREDUCTASE PDZ DOMAIN, NNOS, NITRIC OXIDE SYNTHASE	PEPTIDE RECOGNITION PEPTIDE RECOGNITION, PROTEIN LOCALIZATION	TRANSPORT PROTEIN RHO-GTPASE EXCHANGE FACTOR, TRANSPORT PROTEIN	TRANSPORT PROTEIN RHO-GTPASE EXCHANGE FACTOR, TRANSPORT PROTEIN	GENE REGULATION SON OF SEVENLESS PROTEIN; GUANINE NUCLEOTIDE EXCHANGE FACTOR, GENE REGULATION	SIGNALING PROTEIN 11 ALPHA- HELICES
Coumpound		LECTIN (AGGLUTININ) WHEAT GERM AGGLUTININ (ISOLECTIN 2) 9WGA 3	LECTIN (AGGLUTININ) WHEAT GERM AGGLUTININ (ISOLECTIN 2) 9WGA 3	NEURONAL NITRIC OXIDE SYNTHASE; CHAIN: A; HEPTAPEPTIDE; CHAIN: B;	PSD-95; CHAIN: A; CRIPT; CHAIN: B;	PIX; CHAIN: A;	PIX; CHAIN: A;	HUMAN SOS 1; CHAIN: A;	RHO-GEF VAV; CHAIN: A;
SeqFold Score									
PMF Score		-0.19	-0.20	0.45	69:0	0.75	0.93	1.00	1.00
Verify Score		0.06	0.07	-0.04	0.48	-0.15	0.03	0.18	0.37
PSI- BLAST		1.4e-11	1.7e-10	0.0026	3.4e-12	3.4e-30	2.6e-42	5.1e-36	3.4e-34
End AA		547	178	167	164	987	992	1129	979
Start AA		369	7	9/	<i>L</i> 9	775	187	800	785
Chain D		¥	A	A	Ą	¥	A	¥	A
PDB ID		9wga	9wga	1 b 8q	1be9	1by1	1by1	1dbh	1f5x
SEQ B B Ö		132	132	133	133	133	133	133	133

		N-2 KINASE HCASK, GLGF REPEAT, CHAIN: A, DHR; PDZ DOMAIN, NEUREXIN, SYNDECAN, RECEPTOR CLUSTERING, KINASE		PHOSPHORYLATION PLECKSTRIN (N- TERMINAL HOMOLOGY DOMAIN) MUTANT IPLS 3 WITH LEU GLU (HIS)6 ADDED TO THE C TERMINUS IPLS 4 (INS(G105- LEHHHHHHH)) (NMR, 25 STRUCTURES) IPLS 5 ALPHA-1 RESIDUES 77-171); FINGER, HETERODIMER CHAIN: A; NEURONAL NITRIC OXIDE SYNTHASE
Сош	INTERLEUKIN 16; CHAIN: NULL;	HCASK/LIN-2 PROTBIN; CHAIN: A, B;	HUMAN DISCS LARGE PROTEIN; CHAIN: NULL;	PHOSPHORYLATION PLECKSTRIN (N- TERMINAL PLECKSTRIN HOMOLOGY DOMAIN) MUTANT IPLS 3 WITH LEU GLU (HIS)6 ADDED TO THE C TERMINUS IPLS 4 (INS(G105- LEHHHHHHH)) (NMR, 25 STRUCTURES) IPLS 5 ALPHA-1 SYNTROPHIN (RESIDUES 77-171); CHAIN: A; NEURONAL NITRIC OXIDE SYNTHASE
SeqFold Score				
PMF Score	0.55	0.92	0.93	0.33
Verify Score	0.61	0.58	0.65	0.01
PSI- BLAST	2.6e-17	1.3e-16	6.8e-12	0.0034 5.1e-07
End AA	157	148	153	1144
Start AA	71	71	69	1021
Chain		4		A
PDB TD	1i16	lkwa	1pdr	Ipls Iqav
SEQ NO B	133	133	133	133

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PDB annotation	DOMAIN, NEURONAL NITRIC OXIDE SYNTHASE, NMDA RECEPTOR 2 BINDING	HYDROLASE PDZ DOMAIN, HUMAN PHOSPHATASE, HPTPIE, PTP-BAS, SPECIFICITY 2 OF BINDING		HYDROLASE TETRATRICOPEPTIDE, TRP; HYDROLASE, PHOSPHATASE,	PROTEIN-PROTEIN INTERACTIONS, TPR, 2 SUPER-HELIX, X-RAY	STRUCTURE	HYDROLASE TETRATRICOPEPTIDE, TRP: HYDROLASE, PHOSPHATASE	PROTEIN-PROTEIN INTERACTIONS,	TPR, 2 SUPER-HELIX, X-RAY STRUCTURE	HYDROLASE TETRATRICOPEPTIDE	TRP; HYDROLASE, PHOSPHATASE,	PROTEIN-PROTEIN INTERACTIONS,	TPR, 2 SUPER-HELIX, X-RAY STRUCTURE	HYDROLASE TETRATRICOPEPTIDE,	TRP; HYDROLASE, PHOSPHATASE,	PROTEIN-PROTEIN INTERACTIONS,	TPR, 2 SUPER-HELIX, X-RAY	STRUCTURE	HYDROLASE TETRATRICOPEPTIDE,	TRP; HYDROLASE, PHOSPHATASE,	PROTEIN-PROTEIN INTERACTIONS,	TPR, 2 SUPER-HELIX, X-RAY	STRUCTURE	HYDROLASE TETRATRICOPEPTIDE,
Coumpound	DENSITY PROTEIN 95; CHAIN: A;	TYROSINE PHOSPHATASE (PTP- BAS, TYPE 1); CHAIN: A;		SERINE/THREONINE PROTEIN	PHOSPHATASE 5; CHAIN: NULL;		SERINE/THREONINE PROTEIN	PHOSPHATASE 5;	CHAIN: NULL;	SERINE/THREONINE	PROTEIN	PHOSPHATASE 5;	CHAIN: NULL;	SERINE/THREONINE	PROTEIN	PHOSPHATASE 5;	CHAIN: NULL;	•	SERINE/THREONINE	PROTEIN	PHOSPHATASE 5;	CHAIN: NULL;		SERINE/THREONINE
SeqFold Score																								
PMF Score		0.99		0.00			0.47			0.25				0.77					0.09					0.28
Verify Score		0.75		-0.12			0.10			0.16				0.14					-0.37					-0.09
PSI- BLAST		3.4e-10		6.8e-10			6.8e-14			5.1e-13	-			1e-17					1.3e-07				,	le-09
End		151		249			283			335				343					396					381
Start AA		73		104			149			185				727					235					797
Chain ID		A																	<u>.</u>			•		
PDB JD		3pdz		lai7			la17			la17				la17	<u> </u>				la17					la!/
SEQ DO: NO:		133		134			134			134				134					134				3	134

PDB annotation	TRP; HYDROLASE, PHOSPHATASE, PROTEIN-PROTEIN INTERACTIONS, TPR, 2 SUPER-HELIX, X-RAY STRUCTURE	HYDROLASE TETRATRICOPEPTIDE, TRP, HYDROLASE, PHOSPHATASE, PROTEIN-PROTEIN INTERACTIONS, TPR, 2 SUPER-HELIX, X-RAY STRUCTURE	TRANSFERASE FTASE; FTASE, PFT, PFTASE, FARNESYLTRANSFERASE, FARNESYL 2 TRANSFERASE, RAS, CANCER	SIGNALLING COMPLEX RACI; P67PHOX; SIGNALLING COMPLEX, GTPASE, NADPH OXIDASE, PROTEIN-PROTEIN 2 COMPLEX, TPR MOTIF	SIGNALLING COMPLEX RACI; P67PHOX; SIGNALLING COMPLEX, GTPASE, NADPH OXIDASE, PROTEIN-PROTEIN 2 COMPLEX, TPR MOTIF	SIGNALLING COMPLEX RACI; P67PHOX; SIGNALLING COMPLEX,
Coumpound	PROTEIN PHOSPHATASE 5; CHAIN: NULL;	SERINE/THREONINE PROTEIN PHOSPHATASE 5; CHAIN: NULL;	FARNESYLTRANSFE RASE (ALPHA SUBUNIT); CHAIN: A; FARNESYLTRANSFE RASE (BETA SUBUNIT); CHAIN: B; K-RAS4B PEPTIDE SUBSTRATE; CHAIN: P;	RAS-RELATED C3 BOTULINUM TOXIN SUBSTRATE 1; CHAIN: A; NEUTROPHIL CYTOSOL FACTOR 2 (NCF-2) CHAIN: B;	RAS-RELATED C3 BOTULINUM TOXIN SUBSTRATE 1; CHAIN: A; NEUTROPHIL CYTOSOL FACTOR 2 (NCF-2) CHAIN: B;	RAS-RELATED C3 BOTULINUM TOXIN
SeqFold Score						
PMF Score		-0.14	-0.08	0.15	-0.15	0.13
Verify Score		0.04	90.00	-0.23	0.03	-0.02
PSI- BLAST		6.8e-10	5.1e-10	0.0026	3.4e-11	3.4e-14
End AA		213	422	239	340	389
Start AA		89	150	114	152	229
Chain ID			∢	В	В	В
PDB ID		la17	148d	1e96	1e96	1e96
SEQ NO DE		134	134	134	134	134

PDB annotation	GTPASE, NADPH OXIDASE, PROTEIN-PROTEIN 2 COMPLEX, TPR MOTIF	SIGNALLING COMPLEX RACI; P67PHOX; SIGNALLING COMPLEX, GTPASE, NADPH OXIDASE, PROTEIN-PROTEIN 2 COMPLEX, TPR MOTIF	SIGNALLING COMPLEX RACI; P67PHOX; SIGNALLING COMPLEX, GTPASE, NADPH OXIDASE, PROTEIN-PROTEIN 2 COMPLEX, TPR MOTIF	CHAPERONE HOP, TPR-DOMAIN, PEPTIDE-COMPLEX, HELICAL REPEAT, HSP90, 2 PROTEIN BINDING	CHAPERONE HOP, TPR-DOMAIN, PEPTIDE-COMPLEX, HELICAL REPEAT, HSP90, 2 PROTEIN BINDING	CHAPERONE HOP, TPR-DOMAIN, PEPTIDE-COMPLEX, HELICAL REPEAT, HSP90, 2 PROTEIN BINDING	CHAPERONE HOP, TPR-DOMAIN, PEPTIDE-COMPLEX, HELICAL REPEAT, HSP90, 2 PROTEIN
Coumpound	SUBSTRATE 1; CHAIN: A; NEUTROPHIL CYTOSOL FACTOR 2 (NCF-2) CHAIN: B;	RAS-RELATED C3 BOTULINUM TOXIN SUBSTRATE 1; CHAIN: A; NEUTROPHIL CYTOSOL FACTOR 2 (NCF-2) CHAIN: B;	RAS-RELATED C3 BOTULINUM TOXIN SUBSTRATE 1; CHAIN: A; NEUTROPHIL CYTOSOL FACTOR 2 (NCF-2) CHAIN: B;	TPRZA-DOMAIN OF HOP; CHAIN: A; HSP90-PEPTIDE MEEVD; CHAIN: B;	TPRZA-DOMAIN OF HOP; CHAIN: A; HSP90-PEPTIDE MEEVD; CHAIN: B;	TPRZA-DOMAIN OF HOP; CHAIN: A; HSP90-PEPTIDE MEEVD; CHAIN: B;	TPRZA-DOMAIN OF HOP, CHAIN: A; HSP90-PEPTIDE
SeqFold Score		·			·		
PMF Score		0.12	0.04	0.12	0.21	0.52	0.10
Verify Score		-0.24	-0.15	0.17	-0.13	-0.08	0.25
PSI- BLAST		5.1e-06	3.4e-10	1.7e-10	1.3e-05	5.1e-14	5.2e-10
End AA		481	204	216	242	256	291
Start AA		315	34	105	117	151	167
Chain ID		M	M	V	A	¥	A
PDB ID		1e96	1e96	lelr	1elr	1elr	lelr
SEQ B S		134	134	134	134	134	134

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ıtion		CHAPERONE HOP, TPR-DOMAIN, PEPTIDE-COMPLEX, HELICAL	OTEIN	CHAPERONE HOP, TPR-DOMAIN,	TELICAL	OTEIN	CHAPERONE HOP, TPR-DOMAIN,	TELICAL	OTEIN		CHAPERONE HOP, TPR-DOMAIN,	HELICAL	VII DI L	CHAPERONE HOP TPR-DOMAIN	TEL ICAL	DEPRAT HSC70 2 HSD70 DROTFIN	10,110	CHAPERONE HOP, TPR-DOMAIN,	TELICAL	REPEAT, HSC70, 2 HSP70, PROTEIN		CHAPERONE HOP, TPR-DOMAIN,	TELICAL	REPEAT, HSC70, 2 HSP70, PROTEIN		CHAPERONE HOP, TPR-DOMAIN,	TELICAL	REPEAT, HSC70, 2 HSP70, PROTEIN PINDING	
PDB annotation		HOP, TP MPLEX, I	P90, 2 PR(HOP, TP	MPLEX, I	P90, 2 PR(HOP, TP	MPLEX, 1	P90, 2 PR(HOP, TP	MPLEX, I	r >U, 4 r RN	T HOP TP	MPI FX	C70 2 HG	010, 2 110	HOP, TP	MPLEX, 1	C70, 2 HS		HOP, TP	MPLEX, 1	C70, 2 HS		HOP, TP	MPLEX, 1	C70, 2 HS	
	BINDING	CHAPERONE HOP, TPR-DOM/ PEPTIDE-COMPLEX, HELICAI	REPEAT, HSP90, 2 PROTEIN BINDING	APERONI	PEPTIDE-COMPLEX, HELICAI	REPEAT, HSP90, 2 PROTEIN RINDING	APERONI	PEPTIDE-COMPLEX, HELICAL	REPEAT, HSP90, 2 PROTEIN	BINDING	APERONI	PEPTIDE-COMPLEX, HELICAL	KEFEA1, ROF90, 2 FROTEIN PRINING	A PERONI	PEPTINE, COMPLEX HELICAL	PAT HO	BINDING	APERONI	PEPTIDE-COMPLEX, HELICAL	PEAT, HS	BINDING	APERONI	PEPTIDE-COMPLEX, HELICAL	PEAT, HS	BINDING	APERONI	PEPTIDE-COMPLEX, HELICAL	REPEAT, HS	בייות
ļ	THE PERSON NAMED IN COLUMN 1	田田田田田田田田田田田田田田田田田田田田田田田田田田田田田田田田田田田田田田田	ES ES	E	PEI	E KE	HH	PEI	E E	TIN I	품	PE	2 6	H C	DEI			뚱	PE	<u> </u>	BIL	<u>ਲ</u>	PEI	E	BIL	뚱	PEI	E 6	1
ģun	AIN: B;	AIN OF: A;	DE N.B.	AIN OF	: A ;	DE N. B.	AIN OF	: A ;	日 日 日 日	LIN: B;	AIN OF			IN OF	j di	ς ς Ε σ. τ. τ.	í 1	IN OF	: A, B;	IDE;		IN OF	: A, B;	IDE;		IN OF	: A, B;	IDE;	
Coumpound	MEEVD; CHAIN: B;	TPR2A-DOMAIN OF HOP; CHAIN: A;	HSP90-PEPTIDE MEEVD: CHAIN: B:	TPR2A-DOMAIN OF	HOP; CHAIN: A;	HSP90-PEPTIDE MPEVD: CHAIN: B:	TPRZA-DOMAIN OF	HOP; CHAIN: A;	HSP90-PEPTIDE	MEEVD; CHAIN: B;	TPR2A-DOMAIN OF	HOP; CHAIN: A;	HOP90-PEPTIDE MEEVD: CUADI: B.	TPP 1-DOMAIN OF	HOP. CHAIN: A B.	HOC70 DEDTINE.	CHAIN: C, D;	TPR1-DOMAIN OF	HOP; CHAIN: A, B;	HSC70-PEPTIDE;	CHAIN: C, D;	TPR1-DOMAIN OF	HOP; CHAIN: A, B;	HSC70-PEPTIDE;	CHAIN: C, D;	TPR1-DOMAIN OF	HOP; CHAIN: A, B;	HSC70-PEPTIDE;	うらい
	MEE	TPR2 HOP;	HSP9	TPRZ	HOP;	HSP9	TPRZ	HOP;	HSP9	MEE	TPR2	HOP:	TO Y	TOD	HOP	ָרָלָ מַלָּלָ	CHA	TPR1	HOP;	HSC	CHA	TPR	HOP;	HSC	CHA	TPR1	HOP;	HSC	5
SeqFold Score																													
PMF Score		0.87	-	0.33			0.00				0.18			0.77	:	·		0.80				0.63				90.0			
Verify Score		0.12		-0.30			-0.05				-0.05	-		0 22	77.0			0.55				0.13				-0.50			
PSI- BLAST		3.4e-20		1.7e-12	,		1e-11		•		1.2e-12			3 40.10	71-24.			1.5e-10		. —		3.4e-17				3.4e-12			_
End		343 3.		389 1.			140				183 1.			十	C/7			303				335 3				398 3			_
Start		227		269			35	}			0/			191	101			214				232				274			
Chain TD		A		V	<u> </u>		A				¥			-	<			A				Ą				Ą			
PDB TD		1elr		leir			1elr				lelr				MI21			lelw				lelw				lelw			
SEQ EQ	ğ	134		134	· }		134	;			134				154			134				134				134			

	TEIN	PTS1- A- T, TPR,	PTS1- 4- T, TPR,	PTS1- 4- I, TPR,	PTS1- - I, TPR,	PTS1- I-
otation	, HELICAI ISP70, PRC	IN TEPTOR 1, 11 PROTEIN ,	IN EPTOR 1, 1 PROTEIN 5	N EPTOR 1, 1 PROTEIN 3E REPEA'	N EPTOR 1, 1 PROTEIN 3E REPEA'	N EPTOR 1, I I PROTEIN
PDB annotation	PBPTIDE-COMPLEX, HELICAL REPEAT, HSC70, 2 HSP70, PROTEIN BINDING	SIGNALING PROTEIN PEROXISMORE RECEPTOR 1, PTS1- BP, PEROXIN-5, PTS1 PROTEIN- PEPTIDE COMPLEX, TETRATRICOPEPTIDE REPEAT, TPR, 2 HELICAL REPEAT	SIGNALING PROTEIN PEROXISMORE RECEPTOR 1, PTS1- BP, PEROXIN-5, PTS1 PROTEIN- PEPTIDE COMPLEX, TETRATRICOPEPTIDE REPEAT, TPR, 2 HELICAL REPEAT	SIGNALING PROTEIN PEROXISMORE RECEPTOR 1, PTS1- BP, PEROXIN-5, PTS1 PROTEIN- PEPTIDE COMPLEX, TETRATRICOPEPTIDE REPEAT, TPR, 2 HELICAL REPEAT	SIGNALING PROTEIN PEROXISMORE RECEPTOR 1, PTS1- BP, PEROXIN-5, PTS1 PROTEIN- PEPTIDE COMPLEX, TETRATRICOPEPTIDE REPEAT, TPR, 2 HELICAL REPEAT	SIGNALING PROTEIN PEROXISMORE RECEPTOR 1, PTS1- BP, PEROXIN-5, PTS1 PROTEIN- PEPTIDE COMPLEX,
	REPETIDE- REPEAT, BINDING	SIGNALII PEROXIS BP, PERO PEPTIDE TETRATE 2 HELICA	SIGNALII PEROXIS BP, PERO PEPTIDE TETRATE 2 HELICA	SIGNALIN PEROXISI BP, PERO PEPTIDE TETRATR 2 HELICA	SIGNALIN PEROXISI BP, PERO PEPTIDE TETRATR 2 HELICA	SIGNALIN PEROXISI BP, PERO PEPTIDE
ound	A: A, B; TDE;	AAL 3 SIGNAL R; 5; PTS1- 1G HAIN: C,	AAL 3 SIGNAL R; Y; PTS1- IG HAIN: C,	fal B SIGNAL S; FTS1- G HAIN: C,	IAL SIGNAL S; PTSI- G HAIN: C,	IAL i SIGNAL i; PTS1-
Coumpound	HOP; CHAIN: A, B; HSC70-PEPTIDE; CHAIN: C, D;	PEROXISOMAL TARGETING SIGNAL 1 RECEPTOR; CHAIN: A, B; PTS1- CONTAINING PEPTIDE; CHAIN: C, D:	PEROXISOMAL TARGETING SIGNAL 1 RECEPTOR; CHAIN: A, B; PTS1- CONTAINING PEPTIDE; CHAIN: C,	PEROXISOMAL TARGETING SIGNAL I RECEPTOR; CHAIN: A, B; PTSI- CONTAINING PEPTIDB; CHAIN: C, D;	PEROXISOMAL TARGETING SIGNAL 1 RECEPTOR; CHAIN: A, B; PTS1- CONTAINING PEPTIDE; CHAIN: C, D;	PEROXISOMAL TARGETING SIGNAL 1 RECEPTOR; CHAIN: A, B; PTS1-
SeqFold Score						
PIMF Score		0.54	0.34	0.54	0.19	0.37
Verify Score		0.04	-0.17	-0.14	-0.20	0.07
PSI- BLAST		3.4e-23	6.5e-32	5.1e-28	5.1e-26	5.1e-34
End AA		424	476	485	280	336
Start AA		130	156	233	2	45
Chain ID		V	⋖	∀	V	V
PDB ID		1feh	1fch	1fch	1fch	1fch
SEQ No.		134	134	134	134	134

PDB annotation	C, 2 HELICAL REPEAT C, 2 HELICAL REPEAT	PROTEIN TRANSPORT HELLX- TURN-HELLX TPR-LIKE REPEAT, PROTEIN TRANSPORT	OF CHAPERONE HOP, TPR-DOMAIN, PEPTIDE-COMPLEX, HELICAL REPEAT HSP90, 2 PROTEIN		DF CHAPERONE HOP, TPR-DOMAIN, PEPTIDE-COMPLEX, HELICAL REPEAT, HSP90, 2 PROTEIN S; BINDING	CHAPERONE HOP, TPR-DOMAIN, PEPTIDB-COMPLEX, HELICAL REPEAT, HSC70, 2 HSP70, PROTEIN BINDING		SIGNALING PROTEIN FEROXISMORE RECEPTOR 1, PTS1- BP, PEROXIN-5, PTS1 PROTEIN- PEPTIDE COMPLEX, TETRATRICOPEPTIDE REPEAT, TPR, C, 2 HELICAL REPEAT	IAL PEROXISMORE RECEPTOR 1, PTS1-BP. PEROXIN-5. PTS1 PROTEIN-
Coumpound	CONTAINING PEPTIDE; CHAIN: C, D;	VESICULAR TRANSPORT PROTEIN SEC17; CHAIN: A;	TPR2A-DOMAIN OF HOP; CHAIN: A; HSP90-PEPTIDE	MEEVD; CHAIN: B;	TPR2A-DOMAIN OF HOP; CHAIN: A; HSP90-PEPTIDE MEEVD; CHAIN: B;	TPR1-DOMAIN OF HOP; CHAIN: A, B; HSC70-PEPTIDE; CHAIN: C, D;	TPR1-DOMAIN OF HOP; CHAIN: A, B; HSC70-PEPTIDE; CHAIN: C, D;	PEROXISOMAL TARGETING SIGNAL 1 RECEPTOR; CHAIN: A, B; PTS1- CONTAINING PEPTIDE; CHAIN: C, D;	PEROXISOMAL TARGETING SIGNAL 1 RECEPTOR;
SeqFold Score									
PMF Score		0.11	0.27		0.27	0.40	0.40	0.28	0.28
Verify Score		-0.18	-0.21		-0.21	-0.23	-0.23	-0.40	-0.40
PSI- BLAST		3.4e-07	0.00026		0.00026	0.0052	0.0052	0.00013	0.00013
End AA		385	442		442	440	440	445	445
Start AA		130	371		371	374	374	131	131
Chain ID		Ą	∢		Ą	¥	A	¥	Y
PDB CD		lqqe	lelr		lelr	1elw	lelw	1fch	1fch
8 8 8 8		134	137		137	137	137	137	137

PDB annotation	PEPTIDE COMPLEX, TETRATRICOPEPTIDE REPEAT, TPR, 2 HELICAL REPEAT	SIGNALING PROTEIN PEROXISMORE RECEPTOR 1, PTS1- BP, PEROXIN-5, PTS1 PROTEIN- PEPTIDE COMPLEX, TETRATRICOPEPTIDE REPEAT, TPR, 2 HELICAL REPEAT	SIGNALING PROTEIN PEROXISMORE RECEPTOR 1, PTS1- BP, PEROXIN-5, PTS1 PROTEIN- PEPTIDE COMPLEX, TETRATRICOPEPTIDE REPEAT, TPR, 2 HELICAL REPEAT	SERINE PROTEASE PCPA2; SERINE PROTEASE, ZYMOGEN, HYDROLASE	SERINE PROTEASE PCPA2; SERINE PROTEASE, ZYMOGEN, HYDROLASE	HYDROLASE/HYDROLASE INHIBITOR CARBOXYPEPTIDASE A2, LEECH CARBOXYPEPTIDASE INHIBITOR	
Coumpound	CHAIN: A, B; PTS1- CONTAINING PEPTIDE; CHAIN: C, D;	PEROXISOMAL TARGETING SIGNAL I RECEPTOR; CHAIN: A, B; PTS1- CONTAINING PEPTIDE; CHAIN: C, D;	PEROXISOMAL TARGETING SIGNAL 1 RECEPTOR; CHAIN: A, B; PTS1- CONTAINING PEPTIDE; CHAIN: C, D;	PROCARBOXYPEPTI DASE A2; CHAIN: NULL;	PROCARBOXYPEPTI DASE A2; CHAIN: NULL;	CARBOXYPEPTIDAS E A2; CHAIN: A; METALLOCARBOXY PEPTIDASE INHIBITOR; CHAIN: B	HYDROLASE(C- TERMINAL PEPTIDASE)
SeqFold Score	,			207.01			228.73
PMF Score		0.57	0.57		1.00	1.00	
Verify Score	!	-0.34	-0.34		0.61	0.66	
PSI- BLAST		9.1e-09	9.1e-09	1.4e-95	1.4e-95	3.4e-94	3.4e-89
End		518	518	244	244	244	244
Start		275	275	1	e	E.	
Chain ID		4	4			«	
PDB UU		1fch	1feh	laye	laye	1dtd	1pca
S a S		137	137	138	138	138	138

PDB annotation		•			ANTI-ONCOGENE CELL CYCLE, ANTI-ONCOGENE, REPEAT, ANK REPEAT	COMPLEX (TRANSCRIPTION REGULATION/DNA) GABPALPHA;
Coumpound	PROCARBOXYPEPTI DASE A (E.C.3.4.12.2) 1PCA 3	HYDROLASE(C- TERMINAL PEPTIDASE) PROCARBOXYPEPTI DASE A (E.C.3.4.12.2)	HYDROLASE(C- TERMINAL PEPTIDASE) CARBOXYPEPTIDAS B A (B.C.3.4.17.1) COMPLEX WITH L- PHENYL 2CTC 3 LACTATE (L-O-PHE) 2CTC 4	HYDROLASE(C- TERMINAL PEPTIDASE) CARBOXYPEPTIDAS E A (B.C.3.4.17.1) COMPLEX WITH L- PHENYL 2CTC 3 LACTATE (L-O-PHE) 2CTC 4	TUMOR SUPPRESSOR P16INK4A; CHAIN: NULL;	GA BINDING PROTEIN ALPHA;
SeqFold Score			292.46		:	
PMF Score		1.00		1.00	0.99	1.00
Verify Score		0.62		0.61	0.10	0.11
PSI- BLAST		3.46-89	6.8e-95	6.8e-95	3.4e-24	6.8e-40
End		242	242	242	515	535
Start AA		m.		en .	401	401
Chain ID						B
EDB CD		Ipca	2ctc	2ctc	1a5e	lawc
Og a ç		138	138	138	139	139

PDB annotation	GABPBETA1; COMPLEX (TRANSCRIPTION REGULATION/DNA), DNA-BINDING, 2 NUCLEAR PROTEIN, ETS DOMAIN, ANKYRIN REPEATS, TRANSCRIPTION 3 RACTOR	TUMOR SUPPRESSOR TUMOR SUPPRESSOR, CDK4/6 INHIBITOR, ANKYRIN MOTIF	TUMOR SUPPRESSOR TUMOR SUPPRESSOR, CDK4/6 INHIBITOR, ANKYRIN MOTIF	COMPLEX (KINASE/ANTI- ONCOGENE) CDK6; P16INK4A, MTS1; CYCLIN DEPENDENT KINASE, CYCLIN DEPENDENT KINASE INHIBITORY 2 PROTEIN, CDK, INK4, CELL CYCLE, MULTIPLE TUMOR SUPPRESSOR, 3 MTS1, COMPLEX (KINASE/ANTI- ONCOGENE) HEADER	COMPLEX (INHIBITOR PROTEIN/KINASE) INHIBITOR PROTEIN, CYCLIN-DEPENDENT KINASE, CELL CYCLE 2 CONTROL, ALPHA/BETA, COMPLEX (INHIBITOR PROTEIN/KINASE)	COMPLEX (INHIBITOR PROTEIN/KINASE) INHIBITOR PROTEIN, CYCLIN-DEPENDENT KINASE, CELL CYCLE 2 CONTROL, ALPHA/BETA, COMPLEX (INHIBITOR PROTEIN/KINASE)	COMPLEX (INHIBITOR
Coumpound	CHAIN: A; GA BINDING PROTEIN BETA 1; CHAIN: B; DNA; CHAIN: D, E;	P19INK4D CDK4/6 INHIBITOR; CHAIN: NULL;	P19INK4D CDK4/6 INHIBITOR; CHAIN: NULL;	CYCLIN- DEPENDENT KINASE 6; CHAIN: A; MULTIPLE TUMOR SUPPRESSOR; CHAIN: B;	CYCLIN- DEPENDENT KINASE 6; CHAIN: A; P19INK4D; CHAIN: B;	CYCLIN- DEPENDENT KINASE 6; CHAIN: A; P19INK4D; CHAIN: B;	CYCLIN-
SeqFold Score					,		
PMF Score		0.16	1.00	0.94	0.11	0.04	1.00
Verify Score		-0.36	0.10	-0.07	-0.09	-0.40	0.03
PSI- BLAST		8.5e-31	3.4e-31	1.7e-25	1.5e-27	3.46-29	3.4e-31
End AA		518	536	515	485	518	536
Start AA		371	404	401	350	371	404
Chain Th				В	В	В	В
PDB CD		1bd8	1548	1bi7	1blx	16lx	1blx
S U Š		139	139	139	139	139	139

						,	
PDB annotation	PROTEIN/KINASE) INHIBITOR PROTEIN, CYCLIN-DEPENDENT KINASE, CELL CYCLE 2 CONTROL, ALPHA/BETA, COMPLEX (INHIBITOR PROTEIN/KINASE)	HORMONE/GROWTH FACTOR P18- INK4C; CELL CYCLE INHIBITOR, P18INK4C, TUMOR, SUPPRESSOR, CYCLIN- 2 DEPENDENT KINASE, HORMONE/GROWTH FACTOR	HORMONE/GROWTH FACTOR P18- INK4C; CELL CYCLE INHIBITOR, P18INK4C, TUMOR, SUPPRESSOR, CYCLIN- 2 DEPENDENT KINASE, HORMONE/GROWTH FACTOR	SIGNALING PROTEIN HELIX-TURN- HELIX, ANKYRIN REPEAT	SIGNALING PROTEIN HELIX-TURN- HELIX, ANKYRIN REPEAT	CELL CYCLE INHIBITOR P18- INK4C(INK6); CELL CYCLE INHIBITOR, P18-INK4C(INK6), ANKYRIN REPEAT, 2 CDK 4/6 INHIBITOR	CELL CYCLE INHIBITOR P18- INK4C(INK6); CELL CYCLE INHIBITOR, P18-INK4C(INK6), ANKYRIN REPEAT, 2 CDK 4/6
Coumpound	DEPENDENT KINASE 6; CHAIN: A; P19INK4D; CHAIN: B;	CYCLN- DEPENDENT KINASE 6 INHIBITOR; CHAIN: A;	CYCLN• DEPENDENT KINASE 6 INHIBITOR; CHAIN: A;	CYCLN- DEPENDENT KINASE 4 INHIBITOR B; CHAIN: A;	CYCLIN- DEPENDENT KINASE 4 INHIBITOR B; CHAIN: A;	CYCLIN- DEPENDENT KINASE 6 INHIBITOR; CHAIN: A, B;	CYCLIN- DEPENDENT KINASE 6 INHIBITOR; CHAIN:
SeqFold Score							
PMF Score		0.11	66.0	66.0	0.49	0:00	0.13
Verify Score		-0.33	0.15	0.09	0.10	-0.14	-0.32
PSI- BLAST		1.7e-37	1e-34	5.1e-25	1.7e-19	6.8e-29	1e-36
End		520	538	521	536	486	519
Start		368	401	401	434	347	368
Chain ID		V	∀	¥	V	A	A
PDB ID		1bu9	1bu9	1d9s	1d9s	lihb	lihb
S B S		139	139	139	139	139	139

PDB annotation	INHIBITOR	CELL CYCLE INHIBITOR P18- INK4C(INK6); CELL CYCLE	INHIBITOK, PIS-INK4C(INK6), ANKYRIN REPEAT, 2 CDK 4/6 INHIBITOR	TRANSCRIPTION FACTOR P65;	P50D; TRANSCRIPTION FACTOR,	IKB/NFKB COMPLEX			ANK-REPEAT MYOTROPHIN,	ACETYLATION, NMR, ANK-REPEAT	TRANSCRIPTION REGULATION	TRANSCRIPTION REGULATION,	ANKYRIN REPEATS, CELL-CYCLE	COMPLEX (ANTI-	ONCOGENE/ANKYRIN REPEATS)	P53BP2; ANKYRIN REPEATS, SH3,	P53, TUMOR SUPPRESSOR,	MULTIGENE 2 FAMILY, NUCLEAR	PROTEIN, PHOSPHORYLATION,	DISEASE MUTATION, 3	POLYMORPHISM, COMPLEX (ANTI-	ONCOGENE/ANKYRIN REPEATS)	COMPLEX (ANTI-	ONCOGENE/ANKYRIN REPEATS)	P53BP2; ANKYRIN REPEATS, SH3,	P53, TUMOR SUPPRESSOR,	MULTIGENE 2 FAMILY, NUCLEAR	PROTEIN, PHOSPHORYLATION,	DISEASE MUTATION, 3 POLYMORPHISM, COMPLEX (ANTI-
Coumpound	A, B;	CYCLIN- DEPENDENT	KINASE 0 INHIBITOR; CHAIN: A. B:	NF-KAPPA-B P65	SUBUNIT; CHAIN: A;	NF-KAPPA-B P50D SUBUNIT; CHAIN: C;	I-KAPPA-B-ALPHA;	CHAIN: D;	MYOTROPHIN;	CHAIN: NULL	REGULATORY	PROTEIN SWI6;	CHAIN: A, B;	P53; CHAIN: A;	53BP2; CHAIN: B;								P53; CHAIN: A;	53BP2; CHAIN: B;					
SeqFold Score																			-										
PMF Score		66.0		0.22	·				61.0		0.10			0.80							*-	1	0.78						
Verify Score		0.11		-0.38					0.13		-0.25	-		-0.21									-0.18						
PSI- BLAST		1e-34		1.7e-41					8.5e-26		le-19			3.4e-21							_	30	6.8e-23				-	,	
End AA		538		535	.,				533		537			515								, ;	534						
Start AA		401		342					435		389	_		401								7.5	434						
Chain ID		A		D							∀			<u> </u>								٦	n						
PDB ID		1ihb		likn					lmyo		lsw6			lycs									Tycs						
SEQ Signal Signa		139		139					139		139		,	139								130	139						

		Т			1					_			_		т			_									1
PDB annotation	ONCOGENE/ANKYRIN REPEATS)		OXIDOREDUCTASE OXIDOREDUCTASE,	OXYGENREDUCTASE, DIIRON- CENTRE, 2 FLAVOPROTEINS,	LACTAMASE-FOLD	HYDROLASE GLYOXALASE II; METALLO-HYDROLASE		HYDROLASE HYDROLASE, BETA-	METALLOENZYME		HYDROLASE PROSEGMENT,	PROPERTIDE, INHIBITION, HYDROLASE	HYDROLASE PROSEGMENT,	PROPEPTIDE, INHIBITION,	HYDROI ASE PROSEGMENT	PROPERTIDE INHIBITION.	HYDROLASE	HYDROLASE PROSEGMENT,	PROPEPTIDE, INHIBITION,	HYDROLASE	HYDROLASE II FRAGMENT, CD74	FRAGMENT CYSTEINE	PROTEINASE, CATHEPSIN, MHC	CLASS II, INVARIANT 2 CHAIN,	THYROGLOBULIN TYPE-1 DOMAIN		
Coumpound			RUBREDOXIN:OXY GEN	OXIDOREDUCTASE; CHAIN: A, B		HYDROXYACYLGL UTATHIONE HYDROLASE;	CHAIN: A, B;	METALLO BETA-	CHAIN: A, B;		HUMAN	PROCATHEPSIN L; CHAIN: A;	HUMAN	PROCATHEPSIN L;	HIMAN	PROCATHEPSIN I.:	CHAIN: A;	HUMAN	PROCATHEPSIN L;	CHAIN: A;	CATHEPSIN L:	HEAVY CHAIN;	CHAIN: A, C;	CATHEPSIN L:	LIGHT CHAIN;	CHAIN: B, D; INVARIANT CHAIN:	·
SeqFold Score											497.56		497.56														
PMF Score			0.12			0.27		0.01							1 00	1.00		1.00			0.90						
Verify Score			0.14			-0.03	!	-0.03							0 83	Co.'O		0.83			-0.53						
PSI- BLAST			5.1e-09			6.8e-12		1.4e-12			0		0			>		0			1.7e-17						
End AA			95			96		100			333		333		222	ccc		333			333						
Start			15			8		12			19		19		5	17		21			292						
Chain			Ą			V		A			¥		4			<		A			В						
PDB U		,	1e5d			1qh5		2bc2			1cs8		1cs8		9	ICSO		lcs8			licf						
ğ a ş			141			141		141			142		142	!	5	747		142			142						

	7			·····						,		_			,						
PDB annotation		HYDROLASE II FRAGMENT, CD74 FRAGMENT CYSTEINE PROTEINASE, CATHEPSIN, MHC	CLASS II, INVARIANT 2 CHAIN, THYROGLOBULIN TYPE-1 DOMAIN			SIGNALING PROTEIN G PROTEIN, GTP HYDROLYSIS, KINETIC CRYSTALLOGRAPHY, 2 SIGNALING	PROTEIN	SIGNALING PROTEIN G PROTEIN, GTP HYDROLYSIS, KINETIC	CRYSTALLOGRAPHY, 2 SIGNALING PROTFIN	ENDOCYTOSIS/EXOCYTOSIS G-	PROTEIN, GTPASE, RAB6, VESICULAR TRAFFICKING	G PROTEIN G PROTEIN, RAS, ARF,	ARF6, MEMBRANE TRAFFIC		ENDOCYTOSIS/EXOCYTOSIS G	PROTEIN, VESICULAR TRAFFIC,	GIF HYDROLYSIS, YPI/RAB 2	FROIEIN, ENDOCTIONIS, HYDROLASE	SIGNALING PROTEIN ARF-LIKE	PROTEIN 3, ARLS; PROTEIN-GDP	ARF FAMILY, RAS 2 SUPERFAMILY,
Coumpound	CHAIN: I, J;	CATHEPSIN L: HEAVY CHAIN; CHAIN: A, C;	CATHEPSIN L: LIGHT CHAIN; CHAIN: B, D;	INVARIANT CHAIN; CHAIN: I, J;		TRANSFORMING PROTEIN P21/H-RAS- 1; CHAIN: A;		TRANSFORMING PROTEIN P21/H-RAS-	1; CHAIN: A;	RAB6 GTPASE;	CHAIN: A;	ADP-	RIBOSYLATION EACTOR 6. CTARE	A;	GTP-BINDING	PROTEIN YPT51;	CITALIN: A;		ADP-	KIBOS Y LA JION	PROTEIN 3; CHAIN:
SeqFold Score						53.49			•							-					
PMF Score		0.90						68.0		1.00		1.00			0.63				1.00		
Verify Score		-0.53						0.44		0.80		0.90			0.34				1.00		
PSI- BLAST		1.7e-17	***			6.8e-46	,	6.8e-46		5.1e-48		8.5e-53			3.4e-47				1.7e-45		-
End AA		333				197		197		194		190			197				194		
Start AA		292				77		42		24		14			7 9				23	_	
Chain ID		m				∢].	∢		Ą		∢			V V				∢		
PDB CD		licf				letq.		T Ctd		1d5c		1e0s			lek0	 -			PZI PZI		
SEQ NO:		142			3	143	ç	541		143		143			143				143		

PDB annotation	G-DOMAIN	PROTEIN TRANSPORT GDP- BINDING, MEMBRANE TRAFFICKIN, NON-MYRISTOYLATED IHUR 16	PROTEIN TRANSPORT GDP- BINDING, MEMBRANE TRAFFICKIN, NON-MYRISTOYLATED 1HUR 16	COMPLEX (GTP-BINDING/BEFECTOR) RAS-RELATED PROTEIN RAB3A; COMPLEX (GTP-BINDING/BFFECTOR), G PROTEIN, BFFECTOR, RABCDR, 2 SYNAPTIC EXOCYTOSIS, RAB PROTEIN, RAB3A, RABPHILIN	COMPLEX (GTP-BINDING/EFFECTOR) RAS-RELATED PROTEIN RAB3A; COMPLEX (GTP-BINDING/EFFECTOR), G PROTEIN, EFFECTOR, RABCDR, 2 SYNAPTIC EXOCYTOSIS, RAB PROTEIN, RAB3A, RABPHILIN	HYDROLASE G PROTEIN, VESICULAR TRAFFICKING, GTP HYDROLYSIS, RAB 2 PROTEIN, NEUROTRANSMITTER RELEASE, HYDROLASE	HYDROLASE G PROTEIN, VESICULAR TRAFFICKING, GTP HYDROLYSIS, RAB 2 PROTEIN, NEUROTRANSMITTER RELEASE, HYDROLASE	
Coumpound	Ą;	HUMAN ADP- RIBOSYLATION FACTOR 1; 1HUR 5 CHAIN: A, B; 1HUR 7	HUMAN ADP- RIBOSYLATION FACTOR 1; 1HUR 5 CHAIN: A, B; 1HUR 7	RAB-3A; CHAIN: A; RABPHILIN-3A; CHAIN: B;	RAB-3A; CHAIN: A; RABPHILIN-3A; CHAIN: B;	RAB3A; CHAIN: A;	RAB3A; CHAIN: A;	
SeqFold Score		118.41			51.86		59.67	
PMF Score			1.00	0.27		0.51		
Verify Score			0.64	0.52		0.15		
PSI- BLAST		1e-58	1e-58	1.7e-56	1.7e-56	3.4e-56	3.4e-56	
End		199	196	200	202	197	197	
Start		10	6	13	21	16	16	
Chain D		· ·	4	∢	<	V	V	
PDB U		1hur	1hur	1zbd	1zbd	3rab	3rab	
SEQ SEQ		143	143	143	143	143	143	

PDB annotation	LIPID DEGRADATION PLC-D1; PHOSPHORIC DIESTER HYDROLASE, HYDROLASE, LIPID DEGRADATION, 2 TRANSDUCER, CALCIUM-BINDING, PHOSPHOLIPASE C, 3 PHOSPHOLIPASE C, 3	LIPID DEGRADATION PLC-DI; PHOSPHORIC DIESTER HYDROLASE, HYDROLASE, LIPID DEGRADATION, 2 TRANSDUCER, CALCIUM-BINDING, PHOSPHOLIPASE C, 3 PHOSPHOINOSITIDE-SPECIFIC	RNA-BINDING PROTEIN/RNA TRA PRE-MRNA; SPLICING REGULATION, RNP DOMAIN, RNA COMPLEX	GENE REGULATION/RNA POLY(A) BINDING PROTEIN 1, PABP 1; RRM, PROTEIN-RNA COMPLEX, GENE REGULATION/RNA	GENE REGULATION/RNA POLY(A) BINDING PROTEIN 1, PABP 1; RRM, PROTEIN-RNA COMPLEX, GENE REGULATION/RNA
Coumpound	PHOSPHOINOSITIDE -SPECIFIC PHOSPHOLIPASE C, CHAIN: A, B;	PHOSPHOINOSITIDE -SPECIFIC PHOSPHOLIPASE C, CHAIN: A, B;	SXL-LETHAL PROTEIN; CHAIN: A, B; RNA (5'- R(P*GP*UP*UP*GP* UP*UP*UP*UP*U P*UP*U)- CHAIN: P, Q;	POLYDENYLATE BINDING PROTEIN 1; CHAIN: A, B, C, D, E, F, G, H; RNA (5'- R(*AP*AP*AP*AP*A P*AP*AP*AP*AP *A)-3'); CHAIN: M, N, O, P, O, R, S, T;	POLYDENYLATE BINDING PROTEIN 1; CHAIN: A, B, C, D, E, F, G, H; RNA (5'- R(*AP*AP*AP*AP*A
SeqFold Score					
PMF Score	1.00	1.00	0.62	0.43	0.13
Verify Score	0.29	0.09	-0.14	-0.06	-0.32
PSI- BLAST	3.4e-69	3.4e-69	le-17	1.7e-17	5.1e-21
End	222		86	122	112
Start AA	1	-	==	33	7
Chain ID	Y	м	A	¥	¥
PDB CI	1 dj x	1djx	1b7f	levj	levj
SEQ B B SS	14t	144	147	147	147

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PDB annotation		GENE REGULATION/RNA POLY(A) BINDING PROTEIN 1, PABP 1; RRM, PROTEIN-RNA COMPLEX, GENE REGULATION/RNA	GENE REGULATION/RNA POLY(A) BINDING PROTEIN 1, PABP 1; RRM, PROTEIN-RNA COMPLEX, GENE REGULATION/RNA	GENE REGULATION/RNA POLY(A) BINDING PROTEIN 1, PABP 1; RRM, PROTEIN-RNA COMPLEX, GENE REGULATION/RNA	RNA BINDING PROTEIN RNA- BINDING DOMAIN	NUCLEAR PROTEIN HETEROGENEOUS NUCLEAR RIBONUCLEOPROTEIN A1, NUCLEAR PROTEIN, HNRNP, RBD, RRM, RNP, RNA BINDING, 2 RIBONUCLEOPROTEIN
Coumpound	P*AP*AP*AP*AP *A)-3'); CHAIN: M, N, O, P, Q, R, S, T;	POLYDENYLATE BINDING PROTEIN 1; CHAIN: A, B, C, D, E, F, G, H; RNA (5'- R(*AP*AP*AP*AP*A P*AP*AP*AP*AP*AP *A)-3'); CHAIN: M, N, O, P, Q, R, S, T;	POLYDENYLÁTE BINDING PROTEIN 1; CHAIN: A, B, C, D, E, F, G, H; RNA (5'- R(*AP*AP*AP*AP*A P*AP*AP*AP*AP*AP *A)-3'); CHAIN: M, N, O, P, Q, R, S, T;	POLYDENYLATE BINDING PROTEIN 1; CHAIN: A, B, C, D, E, F, G, H; RNA (5'- R(*AP*AP*AP*AP*A P*AP*AP*AP*AP *A)-3'); CHAIN: M, N, O, P, Q, R, S, T;	HU ANTIGEN C; CHAIN: A;	HNRNP A1; CHAIN: NULL;
SeqFold Score				·		
PMF Score		0.58	0.78	0.80	0.71	0.00
Verify Score		0.18	0.31	0.25	0.35	0.06
PSI- BLAST		1.7e-17	1.7e-17	1.7e-17	3.4e-18	3.46-21
End AA		122	122	122	108	104
Start		33	33	E	32	26
Chain		ф	ř.	н	Ą	
PDB ID		1cvj	1cvj	1cvj	1d8z	lha l
SE E E		147	147	147	147	147

PDB annotation	RNA BINDING PROTEIN RNA- BINDING DOMAIN	COMPLEX (RIBONUCLEOPROTEIN/DNA) HNRNP A1, UPI; COMPLEX (RIBONUCLEOPROTEIN/DNA), HETEROGENEOUS NUCLEAR 2 RIBONUCLEOPROTEIN A1	RNA-BINDING PROTEIN/RNA TRA PRE-MRNA; SPLICING REGULATION, RNP DOMAIN, RNA COMPLEX	RNA-BINDING PROTEIN/RNA TRA PRE-MRNA, SPLICING REGULATION, RNP DOMAIN, RNA COMPLEX	GENE REGULATION/RNA POLY(A) BINDING PROTEIN 1, PABP 1; RRM, PROTEIN-RNA COMPLEX, GENE REGULATION/RNA
Coumpound	HETEROGENEOUS NUCLEAR RIBONUCLEOPROTE IN D0; CHAIN: A;	HETEROGENEOUS NUCLEAR RIBONUCLEOPROTE IN A1; CHAIN: A; 12- NUCLEOTIDE SINGLE-STRANDED TELOMETRIC DNA; CHAIN: B;	SXL-LETHAL PROTEIN; CHAIN: A, B; RNA (5'- R(P*GP*UP*UP*GP* UP*UP*UP*UP*UP*U	SXL-LETHAL PROTEIN; CHAIN: A, B; RNA (5'- R(P*GP*UP*UP*GP* UP*UP*UP*UP*UP*U P*UP*U)- CHAIN: P, Q;	POLYDENYLATE BINDING PROTEIN I; CHAIN: A, B, C, D, E, F, G, H; RNA (5'- R(*AP*AP*AP*AP*A P*AP*AP*AP*AP *A)-3'); CHAIN: M, N, O, P, Q, R, S, T;
SeqFold Score				,	
PMF Score	0.07	0.11	86:0	0.06	0.88
Verify Score	0.04	0.06	0.38	0.06	0.21
PSI- BLAST	5.1e-19	1.4e-22	1.5e-15	8.5e-26	3.4e-17
End AA	101	109	150	145	155
Start AA	32	23	89	7	71
Chain ID	Ą	А	V	∢	щ
PDB CD	1hd1	2up1	1b7f	1b7f	1cvj
S B B B B B	147	147	148	148	148

PDB annotation	GENE REGULATION/RNA POLY(A) BINDING PROTEIN 1, PABP 1; RRM, PROTEIN-RNA COMPLEX, GENE REGULATION/RNA A 4, V,	GENE REGULATIONRNA POLY(A) BINDING PROTEIN 1, PABP 1; RRM, PROTEIN-RNA COMPLEX, GENE REGULATION/RNA A 4, 4,	RNA BINDING PROTEIN RNA- BINDING DOMAIN	RNA BINDING PROTEIN RNA- BINDING DOMAIN	RIBONUCLEOPROTEIN UIA117; RIBONUCLEOPROTEIN, RNP E DOMAIN, SPLICEOSOME	STRUCTURAL PROTEIN PROTEIN C23; RNP, RBD, RRM, RNA BINDING DOMAIN, NUCLEOLUS	RNA BINDING PROTEIN RNA- BINDING DOMAIN	
Coumpound	POLYDENYLATE BINDING PROTEIN 1; CHAIN: A, B, C, D, E, F, G, H; RNA (5'- R(*AP*AP*AP*AP*A P*AP*AP*AP*AP*AP *A)-3'); CHAIN: M, N, O, P, Q, R, S, T;	POLYDENYLATE BINDING PROTEIN 1; CHAIN: A, B, C, D, E, F, G, H; RNA (5'- R(*AP*AP*AP*AP*A P*AP*AP*AP*AP*AP *A)-3'); CHAIN: M, N, O, P, Q, R, S, T;	HU ANTIGEN C; CHAIN: A;	HU ANTIGEN C; CHAIN: A;	UI SMALL NUCLEAR RIBONUCLEOPROTE IN A; CHAIN: NULL;	NUCLEOLIN RBD2; CHAIN: A;	HETEROGENEOUS NUCLEAR RIBONUCLEOPROTE IN DO; CHAIN: A;	RNA-BINDING PROTEIN SEX- LETHAL PROTEIN
SeqFold Score		l						
PMF Score	0.90	0.94	0.35	0.34	0.12	0.18	0.47	0.23
Verify Score	0.39	0.37	0.19	0.21	0.20	67.0	0.33`	-0.14
PSI- BLAST	3.4e-17	3.46-17	1.5e-15	1.7e-15	5.1e-12	1.7e-13	1.2e-19	1.7e-17
End AA	155	155	147	145	146	153	145	149
Start AA	17	17	29	71	49	9/	71	. 19
Chain ID	tr'	н	V	V		¥	V	
PDB ID	lcvj	lcvj	148z	1d9a	1fbt	1fjc	1hd1	lsxl
S a S	148	148	148	148	148	148	148	. 148

PDB annotation		RNA BINDING PROTEIN RNA- BINDING DOMAIN	RNA-BINDING DOMAIN RNA- BINDING DOMAIN, ALTERNATIVE SPLICING	RNA-BINDING PROTEIN SPLICING, U2 SNRNP, RBD, RNA-BINDING PROTEIN	LIPID DEGRADATION PLC-D1; PHOSPHORIC DIESTER HYDROLASE, HYDROLASE, LIPID DEGRADATION, 2 TRANSDUCER, CALCIUM-BINDING, PHOSPHOLIPASE C, 3 PHOSPHOLIPASE C, 3	LIPID DEGRADATION PLC-D1; PHOSPHORIC DIESTER HYDROLASE, HYDROLASE, LIPID DEGRADATION, 2 TRANSDUCER, CALCIUM-BINDING, PHOSPHOLIPASE C, 3 PHOSPHOINOSITIDE-SPECIFIC	LIPID DEGRADATION PLC-D1; PHOSPHORIC DIESTER
Coumpound	(C-TERMINUS, OR SECOND RNA- BINDING DOMAIN 1SXL 3 (RBD-2), RESIDUES 199 - 294 PLUS N-TERMINAL MET) 1SXL 4 (NMR, 17 STRUCTURES) 1SXL 5	MUSASHII; CHAIN: A;	SEX-LETHAL PROTEIN; CHAIN: NULL;	SPLICING FACTOR U2AF 65 KD SUBUNIT; CHAIN: A;	PHOSPHOINOSITIDE -SPECIFIC PHOSPHOLIPASE C, CHAIN: A, B;	PHOSPHOINOSITIDE -SPECIFIC PHOSPHOLIPASE C, CHAIN: A, B;	PHOSPHOINOSITIDE -SPECIFIC
SeqFold Score					519.97	519.97	
PMF Score		0.31	99.0	0.00			1.00
Verify Score		0.56	0.29	-0.09			0.65
PSI- BLAST		5.1e-20	1.5e-15	1.7e-12	0	0	0
End		145	150	145	 793	793	792
Start AA		71	89	70	242	242	259
Chain ID		A		A	¥	∢	A
PDB CD		2mss	2sxl	2u2f	1djx	1djx	1djx
S e S		148	148	148	149	149	149

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PDB annotation	HYDROLASE, HYDROLASE, LIPID DEGRADATION, 2 TRANSDUCER, CALCIUM-BINDING, PHOSPHOLIPASE C, 3 PHOSPHOINOSITIDE-SPECIFIC	LIPID DEGRADATION PLC-D1; PHOSPHORIC DIESTER HYDROLASE, HYDROLASE, LIPID DEGRADATION, 2 TRANSDUCER, CALCIUM-BINDING, PHOSPHOLIPASE C, 3 PHOSPHOINOSITIDE-SPECIFIC	LIPID DEGRADATION PLC-D1; PHOSPHORIC DIESTER HYDROLASE, HYDROLASE, LIPID DEGRADATION, 2 TRANSDUCER, CALCIUM-BINDING, PHOSPHOLIPASE C, 3 PHOSPHOINOSITIDE-SPECIFIC	LIPID DEGRADATION PLC-D1; PHOSPHORIC DIESTER HYDROLASE, HYDROLASE, LIPID DEGRADATION, 2 TRANSDUCER, CALCIUM-BINDING, PHOSPHOLIPASE C, 3 PHOSPHOINOSITIDE-SPECIFIC	LIPID DEGRADATION PLC-D1; PHOSPHORIC DIESTER HYDROLASE, HYDROLASE, LIPID DEGRADATION, 2 TRANSDUCER, CALCIUM-BINDING, PHOSPHOLIPASE C, 3 PHOSPHOINOSITIDE-SPECIFIC	LIPID DEGRADATION PLC-D1; PHOSPHORIC DIESTER
Coumpound	PHOSPHOLIPASE C, CHAIN: A, B;	PHOSPHOINOSITIDE -SPECIFIC PHOSPHOLIPASE C, CHAIN: A, B;	PHOSPHOINOSITIDE -SPECIFIC PHOSPHOLIPASE C, CHAIN: A, B;	PHOSPHOINOSITIDE -SPECIFIC PHOSPHOLIPASE C, CHAIN: A, B;	PHOSPHOINOSITIDE -SPECIFIC PHOSPHOLIPASE C, CHAIN: A, B;	PHOSPHOINOSITIDE -SPECIFIC
SeqFold Score			571.84	571.84		
PMF Score		1.00			00.1	1.00
Verify Score		0.68			0.65	99:0
PSI- BLAST		0	0	0	0	0
End		792	793	793	792	792
Start		259	200	200	201	201
Chain		V	æ	В	м	В.
PDB TD		1djx	1djx	1djx	1djx	1djx
SEQ EQ		149	149	149	149	149

PDB annotation	HYDROLASE, HYDROLASE, LIPID DEGRADATION, 2 TRANSDUCER, CALCIUM-BINDING, PHOSPHOLIPASE C, 3 PHOSPHOINOSITIDE-SPECIFIC	METAL TRANSPORT CALMODULIN, HIGH RESOLITION DISORDER	METAL TRANSPORT CALMODULIN, HIGH RESOLUTION, DISORDER	SIGNAL TRANSDUCTION PROTEIN	PLECKSTRIN, PHOSPHOLIPASE, INOSITOL TRISPHOSPHATE, 2 SIGNAL TRANSDUCTION PROTEIN,	SIGNAL TRANSDUCTION PROTEIN	PLECKSTRIN, PHOSPHOLIPASE, INOSITOI TRISPHOSPHATE 2	SIGNAL TRANSDUCTION PROTEIN,	HYDROLASE	SIGNAL TRANSDUCTION PROTEIN PLECKSTRIN, PHOSPHOLIPASE,	INOSITOL TRISPHOSPHATE, 2	SIGNAL TRANSDUCTION PROTEIN, HYDROLASE	SIGNAL TRANSDUCTION PROTEIN	PLECKSTRIN, PHOSPHOLIPASE,	INOSITOL TRISPHOSPHATE, 2	SIGNAL TRANSDUCTION PROTEIN, HYDROLASE	CALCIUM-BINDING PROTEIN EF-	HAND 1TNX 14	CALCIUM-BINDING PROTEIN EF- HAND 1TNX 14
Coumpound	PHOSPHOLIPASE C, CHAIN: A, B;	CALMODULIN; CHAIN: A:	CALMODULIN; CHAIN: A;	PHOSPHOLIPASE C	DELTA-1; CHAIN: NULL;	PHOSPHOLIPASE C	DELTA-1; CHAIN:			PHOSPHOLIPASE C DELTA-1; CHAIN:	NULL;		PHOSPHOLIPASE C	DELTA-1; CHAIN:	NOLL;		TROPONIN C; 1TNX	4 CHAIN: NULL; 1TNX 5	TROPONIN C; 1TNX 4 CHAIN: NULL;
SeqFold Score										110.09			110.09					*	
PMF Score		0.07	0.07	1.00		1.00											60.0		60:0
Verify Score		0.18	0.18	0.89		68.0							•				0.07		0.07
PSI- BLAST		5.1e-36	5.1e-36	9.1e-29		9.1e-29				9.1e-29			9.1e-29	-			3.4e-34		3.4e-34
End AA		322	322	170		170				170			170				320		320
Start AA		<i>LL</i> 1	177	55		55				55			55				179		179
Chain ID		¥	A																
PDB ID		lexr	lexr	lmai		lmai			1	Imai			1mai				1tmx		1tmx
SEQ NO:		149	149	149		149				149			149				149		149

PDB annotation				CALMODULIN, CALCIUM BINDING, HELIX-LOOP-HELIX, SIGNALLING, 2 COMPLEX(CALCIUM-BINDING PROTEIN/PEPTIDE)	CALMODULIN, CALCIUM BINDING, HELIX-LOOP-HELIX, SIGNALLING, 2 COMPLEX(CALCIUM-BINDING PROTEIN/PEPTIDE)		HYDROLASE/DNA PROTEIN/Z-DNA COMPLEX, HYDROLASE/DNA	HYDROLASE Z-ALPHA-Z-DNA BINDING DOMAIN, RNA-EDITING, Z-DNA 2 RECOGNITION, ADARI, HELIX-TURN-HELIX, HYDROLASE	P21; SOS; COMPLEX (ONCOGENE PROTEIN/EXCHANGE FACTOR), SMALL GTPASE, 2 EXCHANGE FACTOR
Coumpound	1TNX 5	CONTRACTILE SYSTEM PROTEIN TROPONIN C 1TOP 3	CONTRACTILE SYSTEM PROTEIN TROPONIN C 1TOP 3	CALMODULIN; CHAIN: A; RS20; CHAIN: B;	CALMODULIN; CHAIN: A; RS20; CHAIN: B;	•	DOUBLE- STRANDED RNA SPECIFIC ADENOSINE DEAMINASE CHAIN: A, B, C; DNA (5'- D(*TP*CP*GP*CP*G P*CP*G)-3'); CHAIN: D, E, F;	DOUBLE STRANDED RNA ADENOSINE DEAMINASE; CHAIN: A;	H-RAS; CHAIN: R; SON OF SEVENLESS- 1; CHAIN: S;
SeqFold Score									
PMF Score		0.84	0.84	0.33	0.33		0.96	1.00	0.77
Verify Score		0.26	0.26	0.07	0.07		0.47	0.28	0.23
PSI- BLAST		1.4e-34	1.4e-34	3.4e-36	3.4e-36		0.0046	0.0046	2.6e-28
End		320	320	323	323		68	&	909
Start AA		179	179	176	176		32	32	8451
Chain ID				V	A		¥	Ą	
PDB CD		Itop	ltop	lvrk	lvrk		14bj	1qgp	15kd
S B S		149	149	149	149		151	151	153

PDB annotation	P21; SOS; COMPLEX (ONCOGENE PROTEIN/EXCHANGE FACTOR), SMALL GTPASE, 2 EXCHANGE FACTOR	TRANSCRIPTION COOA GENE PRODUCT; CARBON MONOXIDE, HEME SENSOR, CATABOLITE GENE ACTIVATOR 2 PROTEIN	CYTOKINE LCF, CYTOKINE, LYMPHOCYTE CHEMOATTRACTANT FACTOR, PDZ DOMAIN	KINASE HCASK, GLGF REPEAT, DHR; PDZ DOMAIN, NEUREXIN, SYNDECAN, RECEPTOR CLUSTERING, KINASE	SIGNAL TRANSDUCTION HDLG, DHR3 DOMAIN; SIGNAL TRANSDUCTION, SH3 DOMAIN, REPEAT	KINASE RI(ALPHA); REGULATORY SUBUNIT, KINASE	TRANSCRIPTION/DNA COMPLEX (TRANSCRIPTION REGULATION/DNA), DNA-BINDING, CAMP- 2 BINDING, ACTIVATOR	
Coumpound	H-RAS; CHAIN: R; SON OF SEVENLESS- 1; CHAIN: S;	CARBON MONOXIDE OXIDATION SYSTEM TRANSCRIPTION CHAIN: A, B;	INTERLEUKIN 16; CHAIN: NULL;	HCASK/LIN-2 PROTEIN; CHAIN: A, B;	HUMAN DISCS LARGE PROTEIN; CHAIN: NULL;	CAMP DEPENDENT PROTEIN KINASE; CHAIN: NULL;	CATABOLITE GENE ACTIVATOR PROTEIN; CHAIN: A; DNA (5- D(*GP*TP*CP*AP*C P*AP*TP*TP*AP*AP *T)-3'); CHAIN: B; DNA (5- CHAIN: C;	
SeqFold Score								
PMF Score	1.00	0.19	86.0	1.00	0.80	0.19	0.00	
Verify Score	0.53	-0.35	0.24	0.60	0.72	0.02	-0.13	
PSI- BLAST	1e-64	0.00065	3.9e-14	2.6e-16	9.1e-12	6.8e-12	1.2e-16	
End AA	1116	168	650	659	640	414	480	
Start AA	2900	98	579	577	579	256	339	
Chatn ID		¥		Ą			¥	
PDB ID	1bkd	1179	1i16	lkwa	1pdr	lrgs	2cgp	
SEQ NO:	153	153	153	153	153	153	153	

PDB annotation	GENE REGULATION/DNA IRF-2; TRANSCRIPTION FACTOR, IFN INDUCTION, IRF FAMILY	GENE REGULATION/DNA IRF-2; TRANSCRIPTION FACTOR, IFN INDUCTION, IRF FAMILY	GENE REGULATION/DNA IRF-2; TRANSCRIPTION FACTOR, IFN INDUCTION, IRF FAMILY
Coumpound	INTERFERON REGULATORY FACTOR 2; CHAIN: G, H, I, J, K, L; DNA (5'- D(P*AP*AP*GP*TP* GP*AP*AP*GP*(T) DO) CHAIN: A, B, C; DNA (5'- DNA (5'- DNA (5'- DNA (5'- DNA (5'- DR*TP*CP*AP*CP *TP*TP*CP*AP*CP	INTERFERON REGULATORY FACTOR 2; CHAIN: G, H, I, J, K, L; DNA (5'- D(P*AP*AP*GP*TP* GP*AP*AP*GP*(I DO) CHAIN: A, B, C; DNA (5'- D(*TP*TP*CP*AP*CP *TP*TP*CP*AP*C *TP*TP*CP*AP*C P*(IDO) CHAIN: D, E, F;	INTERFERON REGULATORY FACTOR 2; CHAIN: G, H, I, J, K, L; DNA (5'- D(P*AP*AP*GP*TP* GP*AP*AP*GP*(T) DO) CHAIN: A, B, C;
SeqFold Score		103.26	
PMF Score	1.00		96:0
Verify Score	0.23		-0.33
PSI- BLAST	6.8e-32	6.8e-32	1.7e-11
End AA	75	75	29
Start		1	
Chain D	ڻ ت	G	Ð
PDB ID	2irf	2irf	2irf
SEQ D	157	157	158

PDB annotation		P21; SOS; COMPLEX (ONCOGENE PROTEIN/EXCHANGE FACTOR), SMALL GTPASE 2 EXCHANGE	FACTOR P21; SOS; COMPLEX (ONCOGENE PROTEIN/EXCHANGE FACTOR), SMALL GTPASE, 2 EXCHANGE	PACTOR P21; SOS; COMPLEX (ONCOGENE PROTEIN/EXCHANGE FACTOR), SMALL GTPASE, 2 EXCHANGE	SIGNAL TRANSDUCTION PROTEIN	SIGNALING PROTEIN DAPP1, PHISH, BAM32; PLECKSTRIN, 3-PHOSPHOINOSITIDES, INOSITOL TETRAKISPHOSPHATE 2 SIGNAL TRANSDUCTION PROTEIN, ADAPTOR PROTEIN	SIGNALING PROTEIN DAPPI, PHISH, BAM32; PLECKSTRIN, 3-PHOSPHOINOSITIDES, INOSITOL TETRAKISPHOSPHATE 2 SIGNAL TRANSDUCTION PROTEIN, A PACOR BE COMMENTED.	SIGNALING PROTEIN ARF1
Coumpound	DNA (5'- D(*TP*TP*CP*AP*CP *TP*TP*TP*CP*AP*C P*(IDO) CHAIN: D, E, F;	H-RAS; CHAIN: R; SON OF SEVENLESS- 1; CHAIN: S;	H-RAS; CHAIN: R; SON OF SEVENLESS- 1; CHAIN: S;	H-RAS; CHAIN: R; SON OF SEVENLESS-1; CHAIN: S;	BETA-SPECTRIN; 1BTN 4 CHAIN: NULL; 1BTN 5	OR OF OSINE : A;	DUAL ADAPTOR OF PHOSPHOTYROSINE AND 3- CHAIN: A;	GRP1; CHAIN: A;
SeqFold Score		74.57						
PMF Score			1.00	1.00	0.94	0.59	0.53	0.75
Verify Score			0.37	0.05	0.43	0.31	0.31	0.23
PSI- BLAST		2.6e-76	2.6e-76	3.4e-52	9.1e-21	3.9e-07	6.5e-09	5.2e-06
End		315	293	661	491	488		467
Start AA		SI	S23	S31	392	388	385	391
Chain ID						V	¥	V
PDB ID		15kd	15kd	1bkd	1btn	lfao	1168	lfgy
SEQ NO:		159	159	159	159	159	159	159

PDB annotation	GUANINE NUCLEOTIDE EXCHANGE FACTOR AND PH DOMAIN	SIGNAL TRANSDUCTION SON OF SEVENLESS, PLECKSTRIN, SON OF SEVENLESS, SIGNAL TRANSDUCTION	SIGNAL TRANSDUCTION IRS-1; BETA-SANDWHICH, SIGNAL TRANSDUCTION	TE A NICODITECTION ON A GE	REGULATORY FACTOR X; WINGED HELIX, MHC CLASS II	IRANSCRIPTION FACTOR, PROTEIN- 2 DNA COCRYSTAL	STRUCTURE, NOVEL MODE OF DNA RECOGNITION	RNA-BINDING PROTEIN/RNA TRA	REGULATION, RNP DOMAIN, RNA	COMPLEX	•		GENE REGULATION/RNA POLY(A)	BINDING PROTEIN 1, PABP 1; RRM,	PROTEIN-RNA COMPLEX, GENE	REGULATION/RNA				RNA BINDING PROTEIN RNA-
Coumpound		SOS 1; CHAIN: NULL;	INSULIN RECEPTOR SUBSTRATE 1; CHAIN: A, B;	TO CITA SO II	MHC CLASS II TRANSCRIPTION FACTOR HRFX1;	CHAIN: P; DNA (5'- D(*CP*GP*(BRO)UP*	TP*AP*CP*CP*AP*(B RO) CHAIN: D;	SXL-LETHAL	B; RNA (5'-	R(P*GP*UP*UP*GP*	UP*UP*UP*UP*U	P*UP*U)- CHAIN: P, O:	POLYDENYLATE	BINDING PROTEIN	1; CHAIN: A, B, C, D,	E, F, G, H; RNA (5'-	R(*AP*AP*AP*A	P*AP*AP*AP*AP	*A)-3'); CHAIN: M, N,	HU ANTIGEN C;
SeqFold Score																				
PMF Score		0.16	-0.13		00.1			0.12					0.28				_			69.0
Verify Score		0.18	0.18	,,,	0.61			0.43					0.36							0.38
PSI- BLAST		2.6e-10	3.9e-12	000	6.8e-33			5.1e-18					3.4e-19							5.1e-18
End AA		491	511		183			152					154							153
Start AA		399	391	إ	108			47					20							79
Chain			A		<u>م</u>			A					A							A
PDB UD		1pms	lqqg		1dp7			1b7f					Icvj							1d8z
SEQ EQ		159	159		160			161					161							161

Γ	-	T	1												_							
PDB annotation	BINDING DOMAIN	NUCLEAR PROTEIN HETEROGENEOUS NUCLEAR RIBONUCLEOPROTEIN A1, NUCLEAR PROTEIN, HNRNP, RBD, RRM, RNP, RNA BINDING, 2	RNA BINDING PROTEIN RNA- BINDING DOMAIN										RNA BINDING PROTEIN RNA-	BINDING DOMAIN	RNA-BINDING DOMAIN RNA-	BINDING DOMAIN, ALTERNATIVE	SPLICING	COMPLEX	(RIBONUCLEOPROTEIN/DNA)	HNKNY AI, UPI; COMPLEX	HETEROGENEOUS NUCLEAR 2	RIBONUCLEOPROTEIN A1
Coumpound	CHAIN: A;	HNRNP A1; CHAIN: NULL;	HETEROGENEOUS NUCLEAR RIBONUCLEOPROTE IN DO. CHAIN: A.	RNA-BINDING	PROTEIN SEX-	(C-TERMINUS, OR	SECOND RNA-	BINDING DOMAIN	15AL 3 (KBD-2), RESIDUES 199 - 294	PLUS N-TERMINAL	MET) 1SXL 4 (NMR,	17 STRUCTURES)	MUSASHII: CHAIN:	A;	SEX-LETHAL	PROTEIN; CHAIN:	NULL;	HETEROGENEOUS	NUCLEAK	KIBONUCLEOPKOTE IN A1-CHAIN: A-12-	NUCLEOTIDE	SINGLE-STRANDED
SeqFold Score									-							-						
PMF Score		0.57	0.86	0.12									0.46		0.59			0.40				
Verify Score		0.57	0.87	0.17							١		0.72		0.34			0.68				
PSI- BLAST		1e-26	5.1e-24	5.1e-18									5.1e-19		6.8e-17	7.50.2.6		0.8e-2/				
End		153	154	152						-			154		154			153				
Start AA		77	83	74							_		83		80		1	ę				
Chain D			A									,	V			•						
PDB ID		lha1	1hd1	lsxl						-		<u> </u>	2mss		2sxl		\dagger	Idn7				
SEQ No es		161	161	161									191		161		151	101				

PDB annotation		RNA BINDING DOMAIN RNA BINDING DOMAIN, RBD, RNA RECOGNITION MOTIF, RRM, 2 SPLICING INHIBITOR, TRANSLATIONAL INHIBITOR, SEX 3 DETERMINATION, X CHROMOSOME DOSAGE COMPENSATION	CELL ADHESION PROTEIN EPITHELIAL CADHERIN DOMAINS I AND 2, ECAD12; CADHERIN, CELL ADHESION PROTEIN, CALCIUM	TEIN	CELL ADHESION PROTEIN EPITHELIAL CADHERIN DOMAINS 1	AND 2, ECAD12; CADHERIN, CELL	ADHESION PROTEIN, CALCIUM PINIDING PROTEIN	A DE CARRES	CELL ADHESION PROTEIN EPITHELIAL CADHERIN DOMAINS 1	AND 2, ECAD12; CADHERIN, CELL	ADHESION PROTEIN, CALCIUM	TEIN	ON PROTEIN	CG 13	ON PROTEIN	CG 13	ON PROTEIN	ON PROTEIN	ICI 13	THE THEORY IN CONTINUE TO THE
PD		RNA BINDING DOMAIN RIBINDING DOMAIN, RBD, RECOGNITION MOTIF, RRISPLICING INHIBITOR, TRANSLATIONAL INHIBIT DETERMINATION, X CHRCDOSAGE COMPENSATION	CELL ADHESION PROTEIN EPITHELIAL CADHERIN DO AND 2, ECAD12, CADHERI ADHESION PROTEIN, CAL	BINDING PROTEIN	CELL ADHESION PROTEIN EPITHELIAL CADHERIN DO	AND 2, ECAD1	ADHESION PROTEI	ON I ONIGNIA	CELL ADHESION PROTEIN EPITHELIAL CADHERIN DO	AND 2, ECAD1	ADHESION PR	BINDING PROTEIN	CELL ADHESION PROTEIN	CADHERIN INCG 13	CELL ADHESION PROTEIN	CADHERIN INCG 13	CELL ADHESION PROTEIN	CELL ADHESION PROTEIN	CADHERIN INCI 13	10000
Coumpound	TELOMETRIC DNA; CHAIN: B;	SEX-LETHAL; CHAIN: A, B, C;	B-CADHERIN; CHAIN: A, B;		E-CADHERIN; CHAIN: A. B:	`			E-CADHERIN; CHAIN: A. B:				N-CADHERIN; INCG	3	N-CADHERIN; INCG	3	N-CADHERIN; INCI	N-CADHERIN: INCI	3	
SeqFold Score			75.74	•																
PMF Score		0.54			0.94			į	-0.01				0.11		0.49		0.45	0.37		
Verify Score		0.49			0.39			,	0.36				0.57		0.11		-0.12	-0.15		
PSI- BLAST		1.7e-18	8.5e-30		8.5e-30			3	8.5e-09				0.0029		0.00068		0.0037	0.00012		, ,
End		153	337		337				351				226		335		228	337		ڕ
Start		72	122		142				243				142		267		176	270	; i	
Chain ID		A	¥		∢				Α.								В	æ	1	
PDB D		3sxl	ledh		ledh				1egh	,			lncg		lncg		lnci	Inci		
SEQ B B B		161	162		162				162				162		162		162	162	}	

PDB annotation	ADHESION PROTEIN	CELL ADHESION PROTEIN CELL ADHESION PROTEIN	CELL ADHESION PROTEIN CELL	CHII ADITEON PROTEIN	CELL ADHESION PROTEIN CELL ADHESION PROTEIN	CELL ADHESION UVOMORULIN;	CADHERIN, CALCIUM BINDING, CELL ADHESION	CELL ADHESION UVOMORULIN;	CELL ADHESION	CALCIUM-BINDING PROTEIN CALB;	CALCIUM++/PHOSPHOLIPID	BINDING PROTEIN, 2 CALCIUM- BINDING PROTEIN	ENDOCYTOSIS/EXOCYTOSIS	SYNAPTOTAGMIN, C2-DOMAIN,	EXOCYTOSIS,	NEUROTRANSMITTER 2 RELEASE,	ENDOCYTOSIS/EXOCYTOSIS	LIPID DEGRADATION PLC-D1;	PHOSPHORIC DIESTER	HYDROLASE, HYDROLASE, LIPID	DEGRADATION, 2 TRANSDUCER,	CALCTUM-BINDING,	PHOSPHOLIPASE C, 3	PHOSPHOINOSITIDE-SPECIFIC	LIPID DEGRADATION PLC-D1; PHOSPHORIC DIRECTED	HYDROLASE, HYDROLASE, LIPID	DEGRADATION, 2 TRANSDUCER,
Coumpound	CHAIN: A;	N-CADHERIN; CHAIN: A;	N-CADHERIN;	M. CADITEDEN	N-CADHEKIN; CHAIN: A;	EPITHELIAL	CADHERIN; CHAIN: NULL;	EPITHELIAL	CADHERIN; CHAIN: NULL;	PROTEIN KINASE C	(BETA); CHAIN: A, B;		SYNAPTOTAGMIN I;	CHAIN: A;				PHOSPHOINOSITIDE	-SPECIFIC	PHOSPHOLIPASE C,	CHAIN: A, B;				PHOSPHOINOSITIDE - SPECIFIC	PHOSPHOLIPASE C,	CHAIN: A, B;
SeqFold Score																							-			-	
PMF Score		1.00	0.47	71.0	-0.14	0.17		0.42		0.18			0.13					I.00							1.00		
Verify Score		0.39	0.22	0.10	0.18	0.01		-0.01		-0.28			-0.21				,	0.36							0.19		
PSI- BLAST		5.1e-31	8.5e-10	1 70 26	1./e-20	1.2e-06		1e-05		5.2e-10			3.9e-15				, ,	9.1e-76			,				2.6e-76		
End AA		337	345	300	977	232		341		1217			1251				;	1971							807		
Start AA		142	243	20	OC	142		243		1142			1150	_			000	1029		_		_			509		
Chain ID		A	Ą	 	4					A			A					∢							₩	•	
PDB CD		lncj	Incj	120.	IIIC	1suh		1suh		1a25			1byn				1	x(b1							Idjx		
SEQ NG:		162	162	163	707	162		162		163			163				5	<u> </u>					_		163		

Coumpound PDB annotation	CALCIUM-BINDING, PHOSPHOLIPASE C, 3 PHOSPHOINOSITIDE-SPECIFIC	PHOSPHOINOSITIDE LIPID DEGRADATION PLC-D1; -SPECIFIC PHOSPHORIC DIESTER PHOSPHOLIPASE.C, HYDROLASE, HYDROLASE, LIPID DEGRADATION, 2 TRANSDUCER, CALCIUM-BINDING, PHOSPHOLIPASE C, 3 PHOSPHOINOSITIDE-SPECIFIC	PHOSPHOINOSITIDE -SPECIFIC -SPECIFIC -SPECIFIC -SPECIFIC -SPECIFIC -SPECIFIC -SPHOSPHOLID DEGRADATION PLC-D1; -SPECIFIC -SPECIFIC -SPECIFIC -SPECIFIC -SPECIFIC -SPECIFIC	PHOSPHOINOSITIDE LIPID DEGRADATION PLC-D1; -SPECIFIC PHOSPHORIC DIESTER PHOSPHOLIPASE C, HYDROLASE, HYDROLASE, LIPID DEGRADATION, 2 TRANSDUCER, CALCIUM-BINDING, PHOSPHOLIPASE C, 3 PHOSPHOINOSITIDE-SPECIFIC	CALCIUM/PHOSPHO LIPID BINDING PROTEIN	SYNAPTOTAGMIN I (FIRST C2 DOMAIN) (CALB) 1RSY 3	SYNAPTOTAGMIN I (FIRST C2 DOMAIN) (CALB) 1RSY 3
SeqFold Score		CH CH	-SP -SP -SP -SP	H. CH.	CA LIP PR	見ら	E O
PMF Score		1.00	0.92	1.00	0.13	•	
Verify Score		0.21	-0.14	0.24	-0.41		
PSI- BLAST		1.3e-75	1.4e-10	5.2e-76	9.1e-13		
End AA		1261	781		1250 9		
Start AA		1029	526	905	1151	_	
Chain ID		æ	В	В			
PDB ID		1djx	1djx	1djx	lrsy		
SEQ NO:		163	163	163	163		

PDB annotation		TRANSFORMING GROWTH FACTOR OSTEOGENIC PROTEIN-1, HOP-1.	BMP-7; MORPHOGEN,	TRANSFORMING GROWTH	CARTILAGE, GLYCOPROTEIN	TRANSFORMING GROWTH FACTOR OSTEOGENIC PROTEIN-1, HOP-1	BMP-7; MORPHOGEN,	TRANSFORMING GROWTH	FACTOR, CYTOKINE, BONE, 2 CARTILAGE, GLYCOPROTEIN	GROWTH FACTOR TGF-B1;	GROWTH FACTOR, MITOGEN,	GLYCOPROTEIN	GPOWTH BACTOD TGE D1.	CROMMIT FACTOR LAMBOURY	GROWIH FACIOR, MIJOGEN, GLYCOPROTEIN		GROWTH FACTOR TGF-B1;	GROWTH FACTOR, MITOGEN,	GLYCOPROTEIN	CBOWTH EACTOR TOE BETA3.	GROWIN FACTOR IGF-BEIAS;	GI YCOPROTEIN SIGNAL		GROWTH FACTOR TGF-BETA3; GROWTH FACTOR MITOGEN	GLYCOPROTEIN, SIGNAL	
Coumpound	FACTOR; CHAIN: A, B, C, D;	BONE MORPHOGENETIC	PROTEIN-7; CHAIN:	NULL;		BONE MORPHOGENETIC	PROTEIN-7; CHAIN:	NULL;		TRANSFORMING	GROWTH FACTOR-	BETA 1; CHAIN: A, B.	TRANCEORMANG	Chourti EACTOR	BETA 1: CHAIN: A.	B;	TRANSFORMING	GROWTH FACTOR-	BETA 1; CHAIN: A,	TD ANGEODMING	GPOWTH FACTOR	BETA 3: CHAIN:	NULL;	TRANSFORMING GROWTH FACTOR-	BETA 3; CHAIN:	NOLL;
SeqFold Score						88.97				73.65										77.33	70.11				•	
PMF Score		1.00											0.70	2			28.0							0.81		
Verify Score		10.0											0.05	3			0.21							0.38		
PSI- BLAST	,	3.4e-45				3.4e-45				1.3e-37			1 30-37	1.0-20.1			1.7e-31			1 30-27	1.25-27			1.3e-37		
End AA		406				407				407		•	407	ì			407			407	}			407		
Start		301				301		_		290			206	2			302			200	067			296		
Chain ID										Ą			A	Ξ.			¥									7
PDB ID		1bmp				1bmp				1kla			11/12				1kla			i.e.				1tgi	<u> </u>	1
SEQ UO NO:		164				164				164			164	5			164			164	<u> </u>	_		164		

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PDB annotation	GROWTH FACTOR TGF-BETA3; GROWTH FACTOR, MITOGEN, GLYCOPROTEIN, SIGNAL			CYTOKINE CYTOKINE, BONE MORPHOGENETIC PROTEIN, CYSTIN-KNOT, TGFB- 2 FAMILY		COMPLEX (TRANSCRIPTION FACTOR/DNA) BHLH; UASP2(17); TRANSCRIPTION FACTOR, BASIC HELIX LOOP HELIX, 2 COMPLEX (TRANSCRIPTION FACTOR/DNA)	TRANSFERASE FIXL, HEME DOMAIN, CRYSTAL STRUCTURE, PAS FAMILY, TWO- 2 COMPONENT SYSTEM, HISTIDINE KINASE	
Coumpound	TRANSFORMING GROWTH FACTOR- BETA 3; CHAIN: NULL;	GROWTH FACTOR TRANSFORMING GROWTH FACTOR- BETA TWO (TGF-B2) 2TGI 3	GROWTH FACTOR TRANSFORMING GROWTH FACTOR- BETA TWO (TGF-B2) 2TGI 3	BONE MORPHOGENETIC PROTEIN 2 (BMP-2); CHAIN: A;		PHOSPHATE SYSTEM POSITIVE REGULATORY PROTEIN CHAIN: A, B; DNA; CHAIN: C,	SENSOR PROTEIN FIXL; CHAIN: A;	TRANSCRIPTION ACTIVATION/DNA MYOD BASIC- HELIX-LOOP-HELIX (BHLH) DOMAIN
SeqFold Score		00.69						
PMF Score	0.96		0.59	0.99		0.11	0.17	0.04
Verify Score	0.13		0.12	0.42		-0.45	0.04	-0.50
PSI- BLAST	1.4e-31	6.8e-31	6.8e-31	3.4e-48		1.7e-09	0.00026	1.2e-14
End AA	407	407	407	406		113	206	116
Start	298	290	302	300		28	141	51
Chain				V		∀	ď	V
80g 61	1tgi	2tgi	2tgi	Зътр		1a0a	IIdm IIdm	lmdy
SEQ No de	164	164	164	164		165	165	165

		 		,	
PDB annotation		RNA-BINDING PROTBIN/RNA TRA PRB-MRNA; SPLICING REGULATION, RNP DOMAIN, RNA COMPLEX	GENE REGULATION/RNA POLY(A) BINDING PROTEIN 1, PABP 1; RRM, PROTEIN-RNA COMPLEX, GENB REGULATION/RNA	RNA BINDING PROTEIN RNA- BINDING DOMAIN	NUCLEAR PROTEIN HETEROGENEOUS NUCLEAR RIBONUCLEOPROTEIN A1, NUCLEAR PROTEIN, HNRNP, RBD, RRM, RNP, RNA BINDING, 2 RIBONUCLEOPROTEIN
Coumpound	1MDY 3 (RESIDUES 102 - 166) MUTANT WITH CYS 135 REPLACED BY SER 1MDY 4 (C135S) COMPLEXED WITH DNA 1MDY 5 (5'- D(*TP*CP*AP*AP*CP *TP*TP*GP*AP*GP *TP*TP*GP*AP*GP	SXL-LETHAL PROTEIN; CHAIN: A, B; RNA (5'- R(P*GP*UP*UP*GP* UP*UP*UP*UP*U	POLYDENYLATE BINDING PROTEIN 1; CHAIN: A, B, C, D, E, F, G, H; RNA (5'- R(*AP*AP*AP*AP*A P*AP*AP*AP*AP*AP *A)-3'); CHAIN: M, N, O, P, Q, R, S, T;	HU ANTIGEN C; CHAIN: A;	HNRNP AI; CHAIN: NULL;
SeqFold Score					
PMF Score	·	0.87	0.72	0.99	0.07
Verify Score		0.34	0.45	0.67	-0.43
PSI- BLAST		5.1e-27	6.8e-23	1.5e-22	5.1e-35
End AA		227	224	168	160
Start AA		 08	2 8	79	
Chain D		¥	⋖	V	
PDB ID		167f	1cvj	1d8z	lhal
SEQ NO:		166	166	166	166

PDB annotation	NUCLEAR PROTEIN HETEROGENEOUS NUCLEAR RIBONUCLEOPROTEIN A1, NUCLEAR PROTEIN, HNRNP, RBD, RRM, RNP, RNA BINDING, 2 RIBONUCLEOPROTEIN	RNA BINDING PROTEIN RNA- BINDING DOMAIN	COMPLEX (RIBONUCLEOPROTEIN/DNA) HNRNP A1, UP1; COMPLEX (RIBONUCLEOPROTEIN/DNA), HETEROGENEOUS NUCLEAR 2 RIBONUCLEOPROTEIN A1	COMPLEX (RIBONUCLEOPROTEIN/DNA) HNRNP A1, UP1; COMPLEX (RIBONUCLEOPROTEIN/DNA), HETEROGENEOUS NUCLEAR 2 RIBONUCLEOPROTEIN A1	RNA BINDING DOMAIN RNA BINDING DOMAIN, RBD, RNA RECOGNITION MOTIF, RRM, 2 SPLICING INHIBITOR, TRANSLATIONAL INHIBITOR, SEX 3 DETERMINATION, X CHROMOSOME DOSAGE COMPENSATION
Coumpound	HNRNP A1; CHAIN: NULL;	HETEROGENEOUS NUCLEAR RIBONUCLEOPROTE IN DO; CHAIN: A;	HETEROGENEOUS NUCLEAR RIBONUCLEOPROTE IN A1, CHAIN: A; 12- NUCLEOTIDE SINGLE-STRANDED TELOMETRIC DNA; CHAIN: B;	HETEROGENEOUS NUCLEAR RIBONUCLEOPROTE IN A1; CHAIN: A; 12- NUCLEOTIDE SINGLE-STRANDED TELOMETRIC DNA; CHAIN: B;	SEX-LETHAL; CHAIN: A, B, C;
SeqFold Score					
PMF	0.19	0.87	0.15	0.45	0.59
Verify Score	0.22	0.69	-0.15	-0.01	0.26
PSI- BLAST	6.8e-29	3.4e-22	5.1e-38	3.4e-31	8.5e-26
End	221	160	166	221	227
Start	77	83		92	83
Chain ID		A	∢	 	Y
PDB ID	lhal	1hd1	2up1	2up1	3sxl
S E E E	166	166	166	166	166

PDB annotation	CELL ADHESION NEURAL CELL ADHESION	CELL ADHESION NEURAL CELL ADHESION	GROWTH FACTOR/GROWTH FACTOR RECEPTOR FGF, FGFR, IMMUNOGLOBULIN-LIKE, SIGNAL TRANSDUCTION, 2 DIMERIZATION, GROWTH FACTOR/GROWTH FACTOR RECEPTOR	GROWTH FACTOR/GROWTH FACTOR RECEPTOR FGF, FGFR, IMMUNOGLOBULIN-LIKE, SIGNAL TRANSDUCTION, 2 DIMERIZATION, GROWTH FACTOR/GROWTH	FACTOR RECEPTOR	GROWTH FACTOR/GROWTH FACTOR RECEPTOR FGF, FGFR, IMMUNOGLOBULIN-LIKE, SIGNAL TRANSDUCTION, 2 DIMERIZATION, GROWTH FACTOR/GROWTH FACTOR RECEPTOR	GROWTH FACTOR/GROWTH FACTOR RECEPTOR FGF, FGFR, IMMUNOGLOBULIN-LIKE, SIGNAL TRANSDUCTION, 2 DIMERIZATION, GROWTH FACTOR/GROWTH FACTOR RECEPTOR	GROWTH FACTOR/GROWTH FACTOR RECEPTOR FGF, FGFR,
Coumpound	AXONIN-1; CHAIN: A;	AXONIN-1; CHAIN: A;	FIBROBLAST GROWTH FACTOR 2; CHAIN: A, B; FIBROBLAST GROWTH FACTOR RECEPTOR 1;	CHAIN: C, D; FIBROBLAST GROWTH FACTOR 2; CHAIN: A, B; FIBROBLAST GROWTH FACTOR	RECEPTOR 1; CHAIN: C, D;	FIBROBLAST GROWTH FACTOR 2; CHAIN: A, B; FIBROBLAST GROWTH FACTOR RECEPTOR 1; CHAIN: C, D;	FIBROBLAST GROWTH FACTOR 2; CHAIN: A, B; FIBROBLAST GROWTH FACTOR RECEPTOR 1; CHAIN: C, D;	FIBROBLAST GROWTH FACTOR 2;
SeqFold Score								
PMF Score	-0.01	-0.14	1.00	0.59		1.00	1.00	0.70
Verify Score	0.12	0.15	0.01	0.09		0.38	0.18	0.17
PSI- BLAST	2.6e-34	1.7e-08	1.26-17	1.4e-52		1.26-17	5.2e-43	5.1e-52
End AA	307	127	277	246		277	293	246
Start AA	11	29	150	35		150	150	35
Chain ID	¥	¥	ပ	U		Q	Q	Д
PDB ID	lcs6	1cs6	lcvs	lcvs			lcvs	lcvs
SEQ NO:	167	167	167	167		167	167	167

PDB annotation	IMMUNOGLOBULIN-LIKE, SIGNAL TRANSDUCTION, 2 DIMERIZATION, GROWTH FACTOR/GROWTH FACTOR RECEPTOR	CELL ADHESION NCAM; NCAM, IMMUNOGLOBULIN FOLD, GLYCOPROTEIN	GROWTH FACTOR/GROWTH FACTOR RECEPTOR FGF2; FGFR2; IMMUNOGLOBULIN (IG)LIKE DOMAINS BELONGING TO THE I- SET 2 SUBGROUP WITHIN IG-LIKE DOMAINS, B-TREFOIL FOLD	GROWTH FACTOR/GROWTH FACTOR RECEPTOR FGF2; FGFR2; IMMUNOGLOBULN (IG)LIKE DOMAINS BELONGING TO THE I- SET 2 SUBGROUP WITHIN IG-LIKE DOMAINS, B-TREFOIL FOLD	GROWTH FACTOR/GROWTH FACTOR RECEPTOR FGF2; FGFR2; IMMUNOGLOBULIN (IG)LIKE DOMAINS BELONGING TO THE I- SET 2 SUBGROUP WITHIN IG-LIKE DOMAINS, B-TREFOIL FOLD	GROWTH FACTOR/GROWTH FACTOR RECEPTOR FGF1; FGFR1; IMMUNOGLOBULN (IG) LIKE DOMAINS BELONGING TO THE I- SET 2 SUBGROUP WITHIN IG-LIKE
Coumpound	CHAIN: A, B; FIBROBLAST GROWTH FACTOR RECEPTOR 1; CHAIN: C, D;	NEURAL CELL ADHESION MOLECULE; CHAIN: A, B, C, D;	FIBROBLAST GROWTH FACTOR 2; CHAIN: A, B, C, D; FIBROBLAST GROWTH FACTOR RECEPTOR 2; CHAIN: E, F, G, H;	FIBROBLAST GROWTH FACTOR 2; CHAIN: A, B, C, D; FIBROBLAST GROWTH FACTOR RECEPTOR 2; CHAIN: E, F, G, H;	FIBROBLAST GROWTH FACTOR 2; CHAIN: A, B, C, D; FIBROBLAST GROWTH FACTOR RECEPTOR 2; CHAIN: E, F, G, H;	
SeqFold Score						
PMF		0.94	0.84	1.00	0.86	1.00
Verify Score		0.36	0.14	0.14	0.04	0.19
PSI- BLAST		2.6e-18	3.4e-49	6.8e-19	1.7e-52	1.7e-17
End		232	246	297	247	277
Start		54	34	150	34	150
Chain		A	m	ق ا	Ð	ပ
PDB UD		lepf	lev2	lev2	lev2	levt
ğa ş		167	167	167	167	167

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PDB annotation	DOMAINS, B-TREFOIL FOLD	GROWTH FACTOR/GROWTH	FACTOR RECEPTOR FGF1; FGFR1;	IMMUNOGLOBULIN (IG) LIKE	DOMAINS BELONGING TO THE I-	SET 2 SUBGROUP WITHIN IG-LIKE	DOMAINS, B-TREFOIL FOLD	IMMUNE SYSTEM FC-EPSILON RI-	ALPHA; IMMUNOGLOBULIN FOLD,	GLYCOPROTEIN, RECEPTOR, IGE-	BINDING 2 PROTEIN	IMMUNE SYSTEM FC-EPSILON RI-	ALPHA; IMMUNOGLOBULIN FOLD,	GLYCOPROTEIN, RECEPTOR, IGE-	BINDING 2 PROTEIN	IMMUNE SYSTEM, MEMBRANE	PROTEIN CD32; FC RECEPTOR,	IMMUNOGLOULIN, LEUKOCYTE,	CD32	IMMUNE SYSTEM, MEMBRANE	PROTEIN CD32; FC RECEPTOR,	IMMUNOGLOULIN, LEUKOCYTE,	CD32	PHOSPHOTRANSFERASE FGFR1K,	FIBROBLAST GROWTH FACTOR	RECEPTOR 1; TRANSFERASE,	TYROSINE-PROTEIN KINASE, ATP-	BINDING, 2 PHOSPHORYLATION,	RECEPTOR,	PHOSPHOTRANSFERASE	PHOSPHOTRANSFERASE FGFR1K, FIBROBLAST GROWTH FACTOR
Coumpound	RECEPTOR 1; CHAIN: C, D;	FIBROBLAST	GROWTH FACTOR 1;	CHAIN: A, B;	FIBROBLAST	GROWTH FACTOR	RECEPTOR 1; CHAIN: C, D;	HIGH AFFINITY	IMMUNOGLOBULIN	EPSILON RECEPTOR	CHAIN: A;	HIGH AFFINITY	IMMUNOGLOBULIN	EPSILON RECEPTOR	CHAIN: A;	FC RECEPTOR	FC(GAMIMA)RIIA;	CHAIN: A;		FC RECEPTOR	FC(GAMMA)RIIA;	CHAIN: A;		FGF RECEPTOR 1;	CHAIN: A, B;						FGF RECEPTOR 1; CHAIN: A, B;
SeqFold Score																															412.56
PMF Score		0.84						0.55				0.42				0.03				0.92				1.00							
Verify Score		-0.01						0.20				0.46				0.49				0.26				1.00							
PSI- BLAST		le-49						7.8e-08		ı		9.1e-15	·	-		1.2e-07		-		1.3e-16				0							0
End AA		246						126				247				109				245				644							644
Start AA		35						45				54				39				72				346			_				346
Chain D		ပ						A				¥				∀				∢				∢							V
PDB CD		levt						1f2q				1524				1fcg				lfcg				1fgk				_	-	寸	Ifgk
S e S		167						167				167				167				167				167]

PDB annotation	RECEPTOR 1; TRANSFERASE, TYROSINE-PROTEIN KINASE, ATP- BINDING, 2 PHOSPHORYLATION, RECEPTOR, PHOSPHOTRANSFERASE	PHOSPHOTRANSFERASE FGFRIK, FIBROBLAST GROWTH FACTOR RECEPTOR 1; TRANSFERASE, TYROSINE-PROTEIN KINASE, ATP-BINDING, 2 PHOSPHORYLATION, RECEPTOR, PHOSPHOTRANSFERASE	PHOSPHOTRANSFERASE FGFRIK, FIBROBLAST GROWTH FACTOR RECEPTOR 1; TRANSFERASE, TYROSINE-PROTEIN KINASE, ATP- BINDING, 2 PHOSPHORYLATION, RECEPTOR, PHOSPHOTRANSFERASE	PHOSPHOTRANSFERASE C-SRC, P60-SRC; SRC, TYROSINE KINASE, PHOSPHORYLATION, SH2, SH3, 2 PHOSPHOTYROSINE, PROTO- ONCOGENE, PHOSPHOTRANSFERASE	COMPLEX (IMMUNOGLOBULIN/RECEPTOR) IMMUNOGLOBULIN FOLD, TRANSMEMBRANE, GLYCOPROTEIN, RECEPTOR, 2 SIGNAL, COMPLEX (IMMUNOGLOBULIN/RECEPTOR)	COMPLEX (IMMUNOGLOBULIN/RECEPTOR) IMMUNOGLOBULIN FOLD,
Coumpound		FGF RECEPTOR 1; CHAIN: A, B;	FGF RECEPTOR 1; CHAIN: A, B;	TYROSINE-PROTEIN KINASE SRC; CHAIN: NULL;	INTERLEUKIN-1 BETA; CHAIN: A; TYPE 1 INTERLEUKIN-1 RECEPTOR; CHAIN: B;	INTERLEUKIN-1 BETA; CHAIN: A; TYPE 1
SeqFold Score			390.85			
PMF Score		1.00		1.00	0.13	0.40
Verify Score		0.82		0.39	0.09	0.19
PSI- BLAST		0	0	0	2.6e-21	9.1e-38
End AA		643	643	646	245	321
Start AA		343	343	289	=	42
Chain TD		æ	щ		m	æ
PDB U		1fgk	lfgk	1fmk	##	lifb
SEQ No.		167	167	167		167

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PDB annotation	TRANSMEMBRANE, GLYCOPROTEIN, RECEPTOR, 2 SIGNAL, COMPLEX (IMMUNOGLOBULINRECEPTOR)	COMPLEX (IMMUNOGLOBULIN/RECEPTOR) IMMUNOGLOBULIN FOLD, TRANSMEMBRANE, GLYCOPROTEIN, RECEPTOR, 2 SIGNAL, COMPLEX (IMMUNOGLOBULIN/RECEPTOR)	MUSCLE PROTEIN CONNECTIN, NEXTM5; CELL ADHESION, GLYCOPROTEIN, TRANSMEMBRANE, REPEAT, BRAIN, 2 IMMUNOGLOBULIN FOLD, ALTERNATIVE SPLICING, SIGNAL, 3 MUSCLE PROTEIN	TYROSINE KINASE TYROSINE KINASE-INHIBITOR COMPLEX, DOWN-REGULATED KINASE, 2 ORDERED ACTIVATION LOOP		MUSCLE PROTEIN IMMUNOGLOBULIN SUPERFAMILY, I SET, MUSCLE PROTEIN	IMMUNE SYSTEM PS8 NATURAL KILLER CELL RECEPTOR; KIR,
Coumpound	INTERLEUKIN-1 RECEPTOR; CHAIN: B;	NTERLEUKIN-1 BETA; CHAIN: A; TYPE 1 INTERLEUKIN-1 RECEPTOR; CHAIN: B;	TITIN; CHAIN: NULL;	HAEMATOPOETIC CELL KINASE (HCK); CHAIN: A;	MUSCLE PROTEIN TITIN MODULE M5 (CONNECTIN) 1TNM 3 (NMR, MINIMIZED AVERAGE STRUCTURE) 1TNM 4 1TNM 58	TWITCHIN 18TH IGSF MODULE; CHAIN: NULL;	MHC CLASS I NK CELL RECEPTOR
SeqFold Score		89.43					
PMF Score			-0.17	1.00	-0.18	0.41	0.46
Verify Score			0.00	0.43	0.13	0.29	0.12
PSI- BLAST		9.1e-38	8.5e-09	0	8.5e-09	2.6e-07	2.6e-17
End AA		367	127	649	127	110	247
Start AA		42	46	291	46	54	54
Chain ID		В		A		•	A
PDB ID		1itb	Inct	lqcf	1tum	lwit	2dli
SEQ B B SS		167	167	167	167	167	167

PDB annotation	NATURAL KILLER RECEPTOR, INHIBITORY RECEPTOR, 2 IMMUNOGLOBULIN	IMMUNE SYSTEM CD32; RECEPTOR, FC, CD32, IMMUNE SYSTEM	CELL ADHESION PROTEIN NCAM MODULE 2; CELL ADHESION, GLYCOPROTEIN, HEPARIN-	BINDING, GPI-ANCHOR, 2 NEURAL ADHESION MOLECULE,	IMMUNOGLOBULIN FOLD, HOMOPHILIC 3 BINDING, CELL ADHESION PROTEIN	SERUM PROTEIN ACRP30 CIQ TNF	PROTEIN	SERUM PROTEIN ACRP30 C10 TNF	TRIMER ALL-BETA, SERUM PROTEIN		SERUM PROTEIN ACRP30 C1Q TNF	IRIMER ALL-BETA, SERUM PROTEIN		SERUM PROTEIN ACRP30 C1Q TNF	TRIMER ALL-BETA, SERUM		SERUM PROTEIN ACRP30 C1Q TNF TRIMER ALL-BETA, SERUM	PROTEIN	
Coumpound	PRECURSOR; CHAIN: A;	FC GAMMA RIIB; CHAIN: A;	NEURAL CELL ADHESION MOLECULE, LARGE	ISOFORM; CHAIN: A;		30 KD ADIPOCYTE	RELATED PROTEIN CHAIN: A, B, C;	30 KD ADIPOCYTE	COMPLEMENT. RELATED PROTEIN	CHAIN: A, B, C;	30 KD ADIPOCYTE	COMPLEMENT: RELATED PROTEIN	CHAIN: A, B, C;	30 KD ADIPOCYTE	COMPLEMENT-	CHAIN: A, B, C;	30 KD ADIPOCYTE COMPLEMENT-	RELATED PROTEIN	CHAIN: A, B, C;
SeqFold Score								110.60									92.47		
PMF Score		06:0	0.35	, <u>, , , , , , , , , , , , , , , , , , </u>		1.00					1.00			0.99				_	
Verify Score		0.21	0.05			0.76					0.71			0.57					
PSI- BLAST		2.6e-19	1.3e-07			2.6e-45		2.6e-45			1.2e-26			2.6e-39			2.6e-39		
End		249	110			277		277			772			9/2			276		
Start		54	54			145		145			149		1	145			145		
Chain ID		V	¥			¥	•	¥			A			В			В		
PDB U		2fcb	Зпст			1c28		1c28			1c28			1c28			1c28		
SEQ E	Ö	167	167			170		170			170			120			170		

PDB annotation	SERUM PROTEIN ACRP30 CIQ TNF TRIMER ALL-BETA, SERUM PROTEIN	SERUM PROTEIN ACRP30 C1Q TNF TRIMER ALL-BETA, SERUM PROTEIN	SERUM PROTEIN ACRP30 C1Q TNF TRIMER ALL-BETA, SERUM PROTEIN	SERUM PROTEIN ACRP30 CIQ TNF TRIMER ALL-BETA, SERUM PROTEIN	SERPIN ACT; SERPIN, SERINE PROTEASE INHIBITOR, ANTICHYMOTRYPSIN	PROTEIN BINDING PAI-2; SERPIN, PROTEIN BINDING	HYDROLASE/HYDROLASE INHIBITOR PROTEASE-INHIBITOR COMPLEX, SERPIN, ALPHA-1- ANTITRYPSIN, 2 TRYPSIN	
Coumpound	30 KD ADIPOCYTE COMPLEMENT- RELATED PROTEIN CHAIN: A, B, C;	ANTICHYMOTRYPSI N; CHAIN: A, B;	PLASMINOGEN ACTIVATOR INHIBITOR-2; CHAIN: A;	ALPHA-1- ANTITRYPSIN; CHAIN: A; ALPHA-1- ANTITRYPSIN; CHAIN: B; TRYPSIN;	HYDROLASE INHIBITOR(SERINE PROTEINASE) HORSE LEUKOCYTE			
SeqFold Score			73.47		,			
PMF Score	0.82	0.90		1.00	0.89	0.99	0.95	1.00
Verify Score	0.71	0.50		0.35	0.35	0.64	0.31	0.43
PSI- BLAST	6.8e-23	1.3e-32	1.3e-32	3.4e-16	le-47	1.7e-43	8.5e-48	8.5e-48
End	276	276	276	276	167	. 168	167	167
Start AA	159	145	145	164	4	2	4	
Chain D	В	ပ	၁	ပ	4	A	¥	A
PDB ID	1c28	1c28	1c28	1c28	1as4	1by7	lezx	1hle
S B S	170	170	170	170	171	171	171	171

PDB annotation			SERINE PROTEASE INHIBITOR ALPHA-1-PROTEINASE INHIBITOR, ALPHA-1-ANTIPROTEINASE; SERINE PROTEASE INHIBITOR, SERPIN, GLYCOPROTEIN, SIGNAL, 2 POLYMORPHISM, EMPHYSEMA, DISEASE MUTATION, ACUTE PHASE	SERPIN AACT SERPIN, SERINE PROTEINASE INHIBITOR, PARTIAL LOOP 2 INSERTION, LOOP-SHEET POLYMERIZATION, EMPHYSEMA, DISEASE 3 MUTATION, ACUTE PHASE PROTEIN, CONFORMATIONAL DISEASE	SERPIN SERPIN, HEPARIN, INHIBITOR	SERPIN SERPIN, HEPARIN, INHIBITOR	SERPIN SERPIN, HEPARIN, INHIBITOR		
Coumpound	ELASTASE INHIBITOR (HLEI) IHLE 3	SERPIN OVALBUMIN (EGG ALBUMIN) 10VA 3	ALPHA-1- ANTIRYPSIN; CHAIN: A;	ALPHA-1- ANTICHYMOTRYPSI N; CHAIN: A;	ANTITHROMBIN; CHAIN: L, I;	ANTITHROMBIN; CHAIN: L, I;	ANTITHROMBIN; CHAIN: L, I;	HYDROLASE(O-GLYCOSYL) LYSOZYME (B.C.3.2.1.17) 153L3	HYDROLASE(O- GLYCOSYL)
SeqFold Score									
PMF Score		66'0	0.92	0.70	1.00	0.95	0.99	1.00	1.00
Verify Score		0.45	0.43	0.02	0.44	0.22	0.42	0.70	0.70
PSI- BLAST		3.4e-40	8.5e-48	6.8e-46	1.3e-39	3.9e-40	5.1e-39	1e-47	1e-47
End		167	167	167	145	145	167	212	212
Start AA		E	4	4	4	1	3	36	36
Chafn 1D		A	∢	4	I	L	IJ		
PDB ID		lova	lqip	14mn	2ant	2ant	2ant	1531	1531
S B S		171	171	171	171	171	171	172	172

PDB annotation				COMPLEX (TRANSFERASE/PEPTIDE) COMPLEX (TRANSFERASE/PEPTIDE)		COMPLEX (PROTO- ONCOGENE/EARLY PROTEIN) SRC HOMOLOGY 2 DOMAIN; SH2 DOMAIN, SIGNAL TRANSDUCTION, PEPTIDE COMPLEX, 2 COMPLEX
Coumpound	LYSOZYME (E.C.3.2.1.17) 153L 3	HYDROLASE(O-GLYCOSYL) LYSOZYME (B.C.3.2.1.17) 153L 3	HYDROLASE(O- GLYCOSYL) LYSOZYME (E.C.3.2.1.17) 153L 3	C-SRC TYROSINE KINASE; CHAIN: A, B; ACE-FORMYL PHOSPHOTYR-GLU- (N,N-DIPENTYL AMINE); CHAIN: C, D;	TRANSFERASE(PHO SPHOTRANSFERASE) PROTO-ONCOGENE TYROSINE KINASE (B.C.2.7.1.112) 1AB2 3 (SRC HOMOLOGY 2 DOMAIN) (ABELSON, SH2 ABL) 1AB2 4 (NMR, 20 STRUCTURES) 1AB2 5	FYN PROTEIN- TYROSINE KINASE; CHAIN: F; PHOSPHOTYROSYL PEPTIDE; CHAIN: P
SeqFold Score		186.19	186.19			·
PMF Score				0.84	0.87	0.46
Verify Score				0.80	0.55	0.88
PSI- BLAST		1e-47	1e-47	8.5e-19	1.7e-17	5.1e-18
End		212	212	493	496	495
Start AA	;	36	36	393	394	394
Chain ID				A		ĹŦ,
808 CO		1531	1531	1a09	1ab2	laot
g a g		172	172	173	173	173

PDB annotation	(PROTO-ONCOGENE/EARLY PROTEIN)		SH2 DOMAIN PHOSPHATIDYLINOSITOL 3-KINASE REGULATORY ALPHA SH2 DOMAIN, P85ALPHA, PI 3-KINASE, NMR, C TERMINAL SH2 2 DOMAIN	V-SRC SH2 DOMAIN SRC SH2; V-SRC SH2 DOMAIN, PHOSPHOTYROSINE RECOGNITION DOMAIN, PP60 2 SRC SH2 DOMAIN	PHOSPHORYLATION SIGNAL TRANSDUCTION, TYROSINE KINASE, TRANSFERASE, 2 PHOSPHOTRANSFERASE, PHOSPHORYLATION	COMPLEX (PHOSPHOTRANSFERASE/PEPTIDE) PROTEIN-TYROSINE KINASE SH2 DOMAIN, COMPLEX 2 (PHOSPHOTRANSFERASE/PEPTIDE)	SH2 DOMAIN GRB2; GRB2, SH2
Coumpound		HYDROLASE(SH2 DOMAIN) TYROSINE PHOSPHATASE SYP (N-TERMINAL SH2 DOMAIN) 1AYA 3 (PTP1D, SHPTP2) (E.C.3.1.3.48) COMPLEXED WITH THE PEPTIDE 1AYA 4 PDGFR-1009 1AYA 5	P85 ALPHA; CHAIN: NULL;	PP60 V-SRC TYROSINE KINASE TRANSFORMING PROTEIN; CHAIN: NULL;	PSS BLK PROTEIN TYROSINE KINASE; CHAIN: NULL;	SYK PROTEIN TYROSINE KINASE; CHAIN: A; ACETYL- THR-PTR-GLU-THR- LEU-NH2; CHAIN: B;	GROWTH FACTOR
SeqFold Score				-			
PMF Score		0.59	0.49	0.39	0.45	0.09	0.07
Verify Score		0.56	0.36	0.76	0.40	0.42	0.38
PSI- BLAST		2.6e-17	1.3e-19	8.5e-18	3.4e-17	2.6e-18	1.3e-17
End AA		510	511	498	493	511	507
Start AA		400	392	398	388	387	394
Chain D		¥				4	
EDB TD		laya	1bfi	16kI	1blj	1csy	1fhs
SEQ No.		173	173	173	173	173	173

PDB annotation	DOMAIN, PROTEIN NMR, SOLUTION STRUCTURES	COMPLEX (KINASE/PEPTIDE)	COMPLEX (TYROSINE KINASE/PEPTIDE)	COMPLEX (TYROSINE KINASE/PEPTIDE)	
Coumpound	RECEPTOR BOUND PROTEIN-2; CHAIN: NULL;	P56—LCK— TYROSINE KINASE; ILCK 7 CHAIN: A; ILCK 8 TAIL PHOSPHOPEPTIDE TEGQ(PHOSPHO)YQ PQPA; ILCK 14 CHAIN: B; ILCK 15	HUMAN P56 TYROSINE KINASE; ILKK 7 CHAIN: A; ILKK 8 PHOSPHOTYROSYL PEPTIDE AC-PTYR- GLU-GLU-ILE; ILKK II CHAIN: B; ILKK	HUMAN P56 TYROSINE KINASE; ILKK 7 CHAIN: A; ILKK 8 PHOSPHOTYROSYL PEPTIDE AC-PTYR- GLU-GLU-ILE; ILKK 11 CHAIN: B; ILKK 12	PHOSPHOTRANSFER ASE V-SRC TYROSINE KINASE TRANSFORMING PROTEIN (PHOSPHOTYROSIN
SeqFold Score					
PMF Score		0.28	96:0	-0.09	0.40
Verify Score		0.16	0.75	0.32	0.88
PSI- BLAST		5.1e-23	1.2e-16	2.6e-18	1.4e-17
End		493	493	509	493
Start		374	395	395	398
Chain D		A	·	Α	¥
PDB CO		11ck	11184	11kk	1sha
SEQ B B S		173	173	173	173

	<u> </u>		·		
PDB annotation	·	COMPLEX (SIGNAL TRANSDUCTION/PEPTIDE) SH2 DOMAIN, COMPLEX (SIGNAL TRANSDUCTION/PEPTIDE)	TRANSFERASE TRANSFERASE, TYROSINE KINASE, SH3, SH2, ONCOPROTEIN		COMPLEX (BLOOD COAGULATION/INHIBITOR) AUTOPROTHROMBIN IIA; HYDROLASE, SERINE
Coumpound	E ISHA 3 RECOGNITION DOMAIN SH2) (E.C.2.7.1.112) COMPLEX WITH ISHA 4 PHOSPHOPEPTIDE A (TYR-VAL-PRO- MET-LEU, PHOSPHORYLATED TYR) ISHA 5	SHC; CHAIN: A; PHOSPHOPEPTIDE OF THE ZETA CHAIN OF T CELL CHAIN: B;	ABL TYROSINE KINASE; CHAIN: NULL;	SIGNALLING PROTEIN PHOSPHATIDYLINO SITOL 3-KINASE (E.C.2.7.1.137) (N- TERMINAL 2PNA 3 SH2 DOMAIN OF P85-ALPHA SUBUNIT) (NMR, 22 STRUCTURES) 2PNA	ACTIVATED PROTEIN C; CHAIN: C, L; D-PHE-PRO- MAI; CHAIN: P;
SeqFold Score				·	
PMF Score		0.88	0.88	0.35	-0.13
Verify Score		0.74	0.39	0.37	0.16
PSI- BLAST		6.5e-17	1.7e-21	2.6e-18	8.5e-09
End		511	492	512	260
Start AA		394	379	395	168
Chain ID		Y			ı
PDB ID		Itce	2abl	2pna	laut
S B B B S B S		173	173	173	178

PDB annotation	PROTEINASE), PLASMA CALCIUM BINDING, 2 GLYCOPROTEIN, COMPLEX (BLOOD COAGULATIONINHIBITOR)	COMPLEX (BLOOD COAGULATION/INHIBITOR) AUTOPROTHROMBIN IIA; HYDROLASE, SERINE PROTEINASE), PLASMA CALCIUM BINDING, 2 GLYCOPROTEIN, COMPLEX (BLOOD COAGULATION/INHIBITOR)	GLYCOPROTEIN MEMBRANE COFACTOR PROTEIN (MCP); VIRUS RECEPTOR, COMPLEMENT COFACTOR, SHORT CONSENSUS REPEAT, 2 SCR, MEASLES VIRUS, GLYCOPROTEIN	GLYCOPROTEIN MEMBRANE COFACTOR PROTEIN (MCP); VIRUS RECEPTOR, COMPLEMENT COFACTOR, SHORT CONSENSUS REPEAT, 2 SCR, MEASLES VIRUS, GLYCOPROTEIN	GLYCOPROTEIN MEMBRANE COFACTOR PROTEIN (MCP); VIRUS RECEPTOR, COMPLEMENT COFACTOR, SHORT CONSENSUS REPEAT, 2 SCR, MEASLES VIRUS, GLYCOPROTEIN	GLYCOPROTEIN MEMBRANE COFACTOR PROTEIN (MCP); VIRUS RECEPTOR, COMPLEMENT COFACTOR, SHORT CONSENSUS REPEAT, 2 SCR, MEASLES VIRUS,
Coumpound		ACTIVATED PROTEIN C; CHAIN: C, L; D-PHE-PRO- MAI; CHAIN: P;	C, D, E, F;	C, D, E, F;	C, D, B, F,	CD46; CHAIN: A, B,
SeqFold Score						
PMF Score		0.05	0.87	1.00	1.00	1.00
Verify Score		-0.04	0.26	0.71	0.10	0.62
PSI- BLAST		5.2e-16	3.4e-09	2.6e-16	6.5e-20	1.3e-25
End AA		636	211	267	330	387
Start AA		559	113	155	213	272
Chain ID		1	A	A	«	∢
PDB ID		laut	1ckl	1ckl	1ckl	1cki
SEQ D NO:		178	178	178	178	178

PDB annotation	GLYCOPROTEIN	GLYCOPROTEIN MEMBRANE COFACTOR PROTEIN (MCP); VIRUS	RECEPTOR, COMPLEMENT	COFACTOR, SHORT CONSENSUS	REPEAT, 2 SCR, MEASLES VIRUS, GLYCOPROTEIN	GLYCOPROTEIN MEMBRANE	COFACTOR PROTEIN (MCP); VIRUS	RECEPTOR, COMPLEMENT	COFACTOR, SHORT CONSENSUS	REPEAT, 2 SCR, MEASLES VIRUS,	GLYCOPROTEIN	GLYCOPROTEIN MEMBRANE	COFACTOR PROTEIN (MCP); VIRUS	RECEPTOR, COMPLEMENT	COFACTOR, SHORT CONSENSUS	REPEAT, 2 SCR, MEASLES VIRUS,	GLYCOPROTEIN	GLYCOPROTEIN MEMBRANE	COFACTOR PROTEIN (MCP); VIRUS	RECEPTOR, COMPLEMENT	COFACTOR, SHORT CONSENSUS	REPEAT, 2 SCR, MEASLES VIRUS,	GLYCOPROTEIN	GLYCOPROTEIN MEMBRANE	COFACTOR PROTEIN (MCP); VIRUS	RECEPTOR, COMPLEMENT	COFACTOR, SHORT CONSENSUS	REPEAT, 2 SCR, MEASLES VIRUS,	GLYCOPROTEIN	GLYCOPROTEIN MEMBRANE	COFACTOR PROTEIN (MCP); VIRUS RECEPTOR, COMPLEMENT
Coumpound		CD46; CHAIN: A, B, C, D, E, F;				CD46; CHAIN: A, B,	C, D, E, F;					CD46; CHAIN: A, B,	C, D, E, F;	_				CD46; CHAIN: A, B,	C, D, E, F;					CD46; CHAIN: A, B,	C, D, E, F;					CD46; CHAIN: A, B,	C, D, E, F;
SeqFold Score		!												_																	
PMF Score		59:0				0.89						66'0						1.00						66'0						0.99	
Verify Score		0.32				0.51						0.86						0.40						0.43						0.20	
PSI- BLAST		3.4e-10				3.4e-14						9.1e-28						7.8e-23						5.2e-20						2.6e-21	
End		08				445					,	445						505						145						562	
Start		2				332						332						390						40						448	
Chain		¥		_		Ą						Ą						A						¥						٧	
PDB CO		1ckl				1ckl						1ckl			•			1ckl						1ckl						1ckl	
S B S		178				178						178						178						178						178	

PDB annotation	COFACTOR, SHORT CONSENSUS REPEAT, 2 SCR, MEASLES VIRUS, GLYCOPROTEIN	GLYCOPROTEIN MEMBRANE COFACTOR PROTEIN (MCP); VIRUS RECEPTOR, COMPLEMENT COFACTOR, SHORT CONSENSUS REPEAT, 2 SCR, MEASLES VIRUS, GLYCOPROTEIN	SERINE PROTEINASE COAGULATION FACTOR II; COAGULATION FACTOR II; FETOMODULIN, TM, CD141 ANTIGEN; EGR-CMK SERINE PROTEINASE, EGF-LIKE DOMAINS, ANTICOAGULANT COMPLEX, 2 ANTIFIBRINOLYTIC COMPLEX		COMPLEMENT INHIBITOR VCP, SP35; COMPLEMENT, NMR, MODULES, PROTEIN STRUCTURE, VACCINIA VIRUS	COMPLEMENT INHIBITOR VCP, SP35; COMPLEMENT, NMR, MODULES, PROTEIN STRUCTURE, VACCINIA VIRUS	COMPLEMENT INHIBITOR VCP, SP35; COMPLEMENT, NMR, MODULES, PROTEIN STRUCTURE, VACCINIA VIRUS	COMPLEMENT INHIBITOR VCP, SP35; COMPLEMENT, NMR,
Coumpound		CD46; CHAIN: A, B, C, D, B, F;	THROMBIN LIGHT CHAIN; CHAIN: A, B, C, D; THROMBIN HEAVY CHAIN; CHAIN: M, N, O, P; THROMBOMODULI N; CHAIN: I, J, K, L; THROMBIN INHIBITOR L-GLU-L-	GLY-L-ARM; CHAIN: E, F, G, H;	COMPLEMENT CONTROL PROTEIN; CHAIN: A;	COMPLEMENT CONTROL PROTEIN; CHAIN: A;	COMPLEMENT CONTROL PROTEIN; CHAIN: A;	COMPLEMENT CONTROL PROTEIN;
SeqFold Score								
PMF Score		0.77	-0.02		1.00	1.00	0.51	0.93
Verify Score		0.63	0.01		0.71	0.66	0.53	0.35
PSI- BLAST		6.5e-22	3.9e-19		3.9e-21	1.2e-17	5.2e-18	1.2e-11
End AA		93	654		260	268	321	324
Start AA		4	566		154	154	212	213
Chain ID		¥	H	- 	A	Ą	A	A
PDB TD		1cki	1dx5		1e5g	le5g	1e5g	1e5g
SEQ B B S		178	178		178	178	178	178

									
PDB annotation	MODULES, PROTEIN STRUCTURE, VACCINIA VIRUS	COMPLEMENT INHIBITOR VCP, SP35, COMPLEMENT, NMR, MODULES, PROTEIN STRUCTURE, VACCINIA VIRUS	COMPLEMENT INHIBITOR VCP, SP35; COMPLEMENT, NMR, MODULES, PROTEIN STRUCTURE, VACCINIA VIRUS	COMPLEMENT INHIBITOR VCP, SP35; COMPLEMENT, NMR, MODULES, PROTEIN STRUCTURE, VACCINIA VIRUS	COMPLEMENT INHIBITOR VCP, SP35; COMPLEMENT, NMR, MODULES, PROTEIN STRUCTURE, VACCINIA VIRUS	COMPLEMENT INHIBITOR VCP, SP35; COMPLEMENT, NMR, MODULES, PROTEIN STRUCTURE, VACCINIA VIRUS	COMPLEMENT INHIBITOR VCP, SP35; COMPLEMENT, NMR, MODULES, PROTEIN STRUCTURE, VACCINIA VIRUS	COMPLEMENT INHIBITOR VCP, SP35; COMPLEMENT, NMR, MODULES, PROTEIN STRUCTURE, VACCINIA VIRUS	COMPLEMENT INHIBITOR VCP, SP35; COMPLEMENT, NMR, MODULES, PROTEIN STRUCTURE, VACCINIA VIRUS
Coumpound	CHAIN: A;	COMPLEMENT CONTROL PROTEIN; CHAIN: A;	COMPLEMENT CONTROL PROTEIN; CHAIN: A;	COMPLEMENT CONTROL PROTEIN; CHAIN: A;	COMPLEMENT CONTROL PROTEIN; CHAIN: A;	COMPLEMENT CONTROL PROTEIN; CHAIN: A;	COMPLEMENT CONTROL PROTEIN; CHAIN: A;	COMPLEMENT CONTROL PROTEIN; CHAIN: A;	COMPLEMENT CONTROL PROTEIN; CHAIN: A;
SeqFold Score				_					
PMF Score		1.00	1.00	1.00	1.00	66.0	0.99	0.74	1.00
Verify Score		0.75	0.82	0.83	0.44	-0.08	0.63	0.55	0.26
PSI- BLAST		7.8e-27	6.5e-31	5.1e-18	1.7e-17	3.4e-10	9.1e-24	6.8e-11	1.3e-26
End		386	444	444	504	08	145	151	560
Start AA		270	331	332	389	E .	40	40	448
Chain ID		¥	4	∢	¥	V	¥	¥	A
EDB CD		le5g	le5g	le5g	1e5g	le5g	le5g	le5g	1e5g
ğa Ş		178	178	178	178	178	178	178	178

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РДВ аппоtаtion	COMPLEMENT INHIBITOR VCP, SP35; COMPLEMENT, NMR, MODULES, PROTEIN STRUCTURE, VACCINIA VIRUS	COMPLEMENT INHIBITOR VCP, SP35; COMPLEMENT, NMR, MODULES, PROTEIN STRUCTURE, VACCINIA VIRUS	COMPLEMENT INHIBITOR VCP, SP35; COMPLEMENT, NMR, MODULES, PROTEIN STRUCTURE, VACCINIA VIRUS	COMPLEMENT INHIBITOR VCP, SP35; COMPLEMENT, NMR, MODULES, PROTEIN STRUCTURE, VACCINIA VIRUS	BLOOD CLOTTING COMPLEX(SERINE PROTEASE/COFACTOR/LIGAND), BLOOD COAGULATION, 2 SERINE PROTEASE, COMPLEX, CO-FACTOR, RECEPTOR ENZYME, 3 INHIBITOR, GLA, EGF, COMPLEX (SERINE 4 PROTEASE/COFACTOR/LIGAND), BLOOD CLOTTING		
Coumpound	COMPLEMENT CONTROL PROTEIN; CHAIN: A;	COMPLEMENT CONTROL PROTEIN; CHAIN: A;	COMPLEMENT CONTROL PROTEIN; CHAIN: A;	COMPLEMENT CONTROL PROTEIN; CHAIN: A;	BLOOD COAGULATION FACTOR VIIA; CHAIN: L; BLOOD COAGULATION FACTOR VIIA; CHAIN: H; SOLUBLE TISSUE FACTOR; CHAIN: T; 5L15; CHAIN: I;	GLYCOPROTEIN 16TH COMPLEMENT CONTROL PROTEIN (/CCP\$) OF FACTOR H 1HCC 3	GLYCOPROTEIN 16TH COMPLEMENT CONTROL PROTEIN
SeqFold Score							·
PMF Score	1.00	0.42	1.00	1.00	-0.08	0.47	0.46
Verify Score	0.46	0.68	0.53	0.81	0.09	-0.09	0.16
PSI- BLAST	1.2e-23	2.6e-12	6.5e-20	6.8e-18	1.3e-14	5.2e-09	6.5e-13
End AA	93	995	209	210		208	385
Start AA	4	506	97	86	999	154	330
Chain D	¥	A	A	¥	ı		
PDB ID	1e5g	le5g	1 e 5g	1e5g		1hcc	1hcc
S B S	178	821	178	178	178	178	178

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РDВ annotation							
Coumpound	(/CCP\$) OF FACTOR H 1HCC 3	GLYCOPROTEIN 16TH COMPLEMENT CONTROL PROTEIN (/CCP\$) OF FACTOR H 1HCC 3	GLYCOPROTEIN 16TH COMPLEMENT CONTROL PROTEIN (/CCPS) OF FACTOR H 1HCC 3	GLYCOPROTEIN 16TH COMPLEMENT CONTROL PROTEIN (/CCPS) OF FACTOR H 1HCC 3	GLYCOPROTEIN 16TH COMPLEMENT CONTROL PROTEIN (/CCP\$) OF FACTOR H 1HCC 3	GLYCOPROTEIN FACTOR H, 15TH AND 16TH C. MODULE PAIR (NMR, MINIMIZED 1HFHA 1 AVERAGED STRUCTURE) 1HFH 4 1HFHA 5	GLYCOPROTEIN FACTOR H, 15TH AND 16TH C-
SeqFold Score							
PMF Score		0.70	0.95	0.01	0.13	0.94	0.92
Verify Score		0.71	0.27	-0.64	0.10	0.38	0.46
PSI- BLAST		3.9e-12	3.9e-11	1.2e-07	2.6e-15	1.7e-10	5.1e-13
End AA		94	443	35	559	267	444
Start AA		38	390	4	503	151	328
Chain							
PDB CD		lhcc	lhcc	Ihcc	lhcc	Thin	1hfh
SEQ B B S		178	178	178	178	178	178

PDB annotation					
Coumpound	MODULE PAIR (NMR, MINIMIZED 1HFHA 1 AVERAGED STRUCTURE) 1HFH 4 1HFHA 5	GLYCOPROTEIN FACTOR H, 15TH AND 16TH C- MODULE PAIR (NMR, MINIMIZED 1HFHA 1 AVERAGED STRUCTURE) 1HFH 4 1HFHA 5	GLYCOPROTEIN FACTOR H, 15TH AND 16TH C- MODULE PAIR (NMR, MINIMIZED 1HFHA 1 AVERAGED STRUCTURE) 1HFH 4	GLYCOPROTEIN FACTOR H, 15TH C- MODULE PAIR (NMR, MINIMIZED AVERAGED 1HFIA 1 STRUCTURE) 1HFI 4	GLYCOPROTEIN FACTOR H, 15TH C- MODULE PAIR (NMR, MINIMIZED
SeqFold Score		83.97			
PMF Score			0.86	0.95	0.96
Verify Score			0.60	0.55	0.74
PSI- BLAST		5.1e-13	3.4e-11	1.3e-10	1.3e-13
End AA		444	208	209	386
Start AA		328	97	154	330
Chain ID					
PDB ID		1hfh	1hfh	1h.fi	lhfi
SEQ NO:		178	178	178	178

PDB annotation						GLYCOPROTEIN GLYCOPROTEIN	MEMBRANE ADHESION SHORT
Coumpound	AVERAGED IHFIA 1 STRUCTURE) 1HFI 4 1HFIA 5	GLYCOPROTEIN FACTOR H, 15TH C- MODULE PAIR (NMR, MINIMIZED AVERAGED 1HFIA 1 STRUCTURE) 1HFI 4 1HFIA 5	GLYCOPROTEIN FACTOR H, 15TH C- MODULE PAIR (NMR, MINIMIZED AVERAGED 1HFIA 1 STRUCTURE) 1HF1 4 1HFIA 5	GLYCOPROTEIN FACTOR H, 15TH C- MODULE PAIR (NMR, MINIMIZED AVERAGED 1HFIA 1 STRUCTURE) 1HFI 4 1HFIA 5	GLYCOPROTEIN FACTOR H, 15TH C- MODULE PAIR (NMR, MINIMIZED AVERAGED 1HFIA 1 STRUCTURE) 1HFI 4 1HFIA 5	LAMININ; CHAIN: NULL;	HUMAN BETA2-
SeqFold Score				1			
PMF		99.0	0.65	0.18	0.59	-0.18	1.00
Verify Score		0.87	0.59	0.24	0.24	0.13	0.54
PSI- BLAST		6.5e-12	5.2e-12	1e-07	1e-16	6.5e-14	1.7e-29
End		93	44	36	559	639	329
Start		38	390	4	503	532	116
Chain ID							A
PDB U		141	lhfi	Ihfi	1hf	1klo	1qub
SEQ D		178	178	178	178	178	178

PDB annotation	CONSENSUS REPEAT, SUSHI, COMPLEMENT CONTROL PROTEIN, 2 N-GLYCOSYLATION, MULTI- DOMAIN. MEMBRANE A DHESION	MEMBRANE ADHESION SHORT CONSENSUS REPEAT, SUSHI, COMPLEMENT CONTROL PROTEIN, 2 N-GLYCOSYLATION, MULTI-	MEMBRANE ADHESION SHORT CONSENSUS REPEAT, SUSHI, COMPLEMENT CONTROL PROTEIN, 2 N-GLYCOSYLATION, MULTI- DOMAIN, MEMBRANE ADHESION	MEMBRANE ADHESION SHORT CONSENSUS REPEAT, SUSHI, COMPLEMENT CONTROL PROTEIN, 2 N-GLYCOSYLATION, MULTI- DOMAIN, MEMBRANE ADHESION	MEMBRANE ADHESION SHORT CONSENSUS REPEAT, SUSHI, COMPLEMENT CONTROL PROTEIN, 2 N-GLYCOSYLATION, MULTI- DOMAIN, MEMBRANE ADHESION	MEMBRANE ADHESION SHORT CONSENSUS REPEAT, SUSHI, COMPLEMENT CONTROL PROTEIN, 2 N-GLYCOSYLATION, MULTI-	MEMBRANE ADHESION SHORT CONSENSUS REPEAT, SUSHI, COMPLEMENT CONTROL PROTEIN, 2 N-GLYCOSYLATION, MULTI- DOMAIN, MEMBRANE ADHESION
Coumpound	GLYCOPROTEIN I; CHAIN: A;	HUMAN BETA2- GLYCOPROTEIN I; CHAIN: A;	HUMAN BETA2- GLYCOPROTEIN I; CHAIN: A;	HUMAN BETA2- GLYCOPROTEIN I; CHAIN: A;	HUMAN BETA2- GLYCOPROTEIN I; CHAIN: A;	HUMAN BETA2- GLYCOPROTEIN I; CHAIN: A;	HUMAN BETA2- GLYCOPROTEIN I; CHAIN: A;
SeqFold Score					190.64		
PMF Score		1.00	1.00	0.99		1.00	1.00
Verify Score		0.74	0.29	0.06		0.53	0.49
PSI- BLAST		1e-27	3.4e-31	1.7e-34	8.5e-42	8.5e-42	1.7e-25
End AA		443	503	267	631	586	350
Start AA		212	272	2	329	331	40
Chain ID		¥	Ą	¥	¥	V	A
PDB CI		1qub	1qub	lqub	lqub	lqub	lqub
SEQ NO:		178	178	178	178	178	178

							
PDB annotation	MEMBRANE ADHESION SHORT CONSENSUS REPEAT, SUSHI, COMPLEMENT CONTROL PROTEIN, 2 N-GLYCOSYLATION, MULTI- DOMAIN, MEMBRANE ADHESION	COMPLEMENT INHIBITOR SP35, VCP, VACCINIA VIRUS SP35; COMPLEMENT INHIBITOR, COMPLEMENT MODULE, SCR, SUSHI DOMAIN, 2 MODULE PAIR	COMPLEMENT INHIBITOR SP35, VCP, VACCINIA VIRUS SP35; COMPLEMENT INHIBITOR, COMPLEMENT MODULE, SCR, SUSHI DOMAIN, 2 MODULE PAIR	COMPLEMENT INHIBITOR SP35, VCP, VACCINIA VIRUS SP35; COMPLEMENT INHIBITOR, COMPLEMENT MODULE, SCR, SUSHI DOMAIN, 2 MODULE PAIR	COMPLEMENT INHIBITOR SP35, VCP, VACCINIA VIRUS SP35; COMPLEMENT INHIBITOR, COMPLEMENT MODULE, SCR, SUSHI DOMAIN, 2 MODULE PAIR	COMPLEMENT INHIBITOR SP35, VCP, VACCINIA VIRUS SP35; COMPLEMENT INHIBITOR, COMPLEMENT MODULE, SCR, SUSHI DOMAIN, 2 MODULE PAIR	COMPLEMENT INHIBITOR SP35, VCP, VACCINIA VIRUS SP35; COMPLEMENT INHIBITOR, COMPLEMENT MODULE, SCR,
Coumpound	HUMAN BETA2- GLYCOPROTEIN I; CHAIN: A;	VACCINIA VIRUS COMPLEMBNT CONTROL PROTEIN; CHAIN: NULL;	VACCINIA VIRUS COMPLEMENT CONTROL PROTEIN; CHAIN: NULL;				
SeqFold Score						91.05	
PMF Score	0.19	1.00	0.65	86.0	0.82		1.00
Verify Score	-0.01	09.0	0.19	0.81	0.34		0.17
PSI- BLAST	6.8e-19	5.1e-16	6.8e-13	5.1e-13	3.4e-15	5.1e-16	5.1e-16
End	659	268	325	385	444	504	502
Start	448	153	211	270	330	388	390
Chain	4						
PDB CD	1qub	lwc	lwc	lwc	lvvc	lvvc	lwc
S e S	178	178	178	178	178	178	178

PDB annotation	SUSHI DOMAIN, 2 MODULE PAIR	COMPLEMENT INHIBITOR SP35, VCP, VACCINIA VIRUS SP35;	COMPLEMENT INHIBITOR,	COMPLEMENT MODULE, SCR,	SUSHI DOMAIN, 2 MODULE PAIR	COMPLEMENT INFIBITOR SESS, VCP. VACCINIA VIRUS SP35:	COMPLEMENT INHIBITOR,	COMPLEMENT MODULE, SCR, SUSHI DOMAIN, 2 MODULE PAIR	COMPLEMENT INHIBITOR SP35,	VCP, VACCINIA VIRUS SP35;	COMPLEMENT INHIBITOR,	COMPLEMENT MODULE, SCR,	SUSHI DOMAIN, 2 MODULE PAIR	COMPLEMENT INHIBITOR SP35,	VCP, VACCINIA VIRUS SP35;	COMPLEMENT INHIBITOR,	COMPLEMENT MODULE, SCR,	SUSHI DOMAIN, 2 MODULE PAIR	BLOOD COAGULATION FACTOR	STUART FACTOR; BLOOD	COAGULATION FACTOR, SERINE	PROTEINASE, EPIDERMAL 2 GROWTH RACTOR 1 IKE DOMAIN	North Market Committee Com						
Coumpound		VACCINIA VIRUS COMPLEMENT	CONTROL PROTEIN;	CHAIN: NULL;	VACCINITA MBITE	VACCINIA VIRUS	CONTROL PROTEIN;	CHAIN: NULL;	VACCINIA VIRUS	COMPLEMENT	CONTROL PROTEIN;	CHAIN: NULL;		VACCINIA VIRUS	COMPLEMENT	CONTROL PROTEIN;	CHAIN: NULL;		BLOOD	COAGULATION	FACTOR XA; CHAIN:	Ľ, Ç,	LECTIN	(AGGLUTININ)	WHEAT GERM	AGGLUTININ	(ISOLECTIN 2) 9WGA 3	LECTIN	(AUGLOTHNIN)
SeqFold Score											•	•																	
PMF		86.0			70 0	0.80			0.17					99.0					-0.09				-0.18					0.15	
Verify Score		0.48			0.53	0.33			0.43					0.32					0.40				0.27					0.00	
PSI- BLAST		3.4e-09			170.16	1./6-10			3.4e-10					3.4e-16					6.8e-10				6.8e-12					3.4e-12	
End		152			250	000			624					208					260				506					922	
Start AA		40			9440	ŝ			505					24					178				323					503	
Chain ID						-													<u>.</u>				A					V	
PDB TD		lvvc			1.	IAAC			lvvc					lvvc					lxka				9wga)				9wga	
SEQ D NO:		178			170	0 7			178					178					178				178					178	

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PDB annotation		TRANSFERASE BRUTON'S AGAMMAGLOBULINEMIA TYROSINE KINASE, BTK; TRANSFERASE, PH DOMAIN, BTK MOTIF, ZINC BINDING, X-LINKED 2 AGAMMAGLOBULINEMIA, TYROSINE-PROTEIN KINASE	SIGNAL TRANSDUCTION PROTEIN	SIGNALING PROTEIN DAPP1, PHISH,	BAM32; PLECKSTRIN, 3-	PHOSPHOINOSI LIDES, INOSI I OL	TETRAKISPHOSPHATE 2 SIGNAL	ADAPTOR PROTEIN,	SIGNALING PROTEIN DAPPI, PHISH,	BAM32; PLECKSTRIN, 3-	PHOSPHOINOSITIDES, INOSITOL	TETRAKISPHOSPHATE 2 SIGNAL	I KANSDOCTION PROTEIN, ADAPTOR PROTEIN	SIGNALING PROTEIN ARF1	GUANINE NUCLEOTIDE EXCHANGE	FACTOR AND PH DOMAIN	SIGNAL TRANSDUCTION SON OF	SEVENLESS; PLECKSTRIN, SON OF	SEVENLESS, SIGNAL TRANSDUCTION
Coumpound	WHEAT GERM AGGLUTININ (ISOLECTIN 2) 9WGA 3	BRUTON'S TYROSINB KINASE; CHAIN: A, B;	BETA-SPECTRIN; 1BTN 4 CHAIN: NULL; 1BTN 5	DUAL ADAPTOR OF	PHOSPHOTYROSINE	AND 3- CHAIN: A;			DUAL ADAPTOR OF	PHOSPHOTYROSINE	AND 3- CHAIN: A;			GRP1; CHAIN: A;	•		SOS 1; CHAIN:	NOLL;	
SeqFold Score																			
PMF Score		0.47	0.57	1.00					1.00					0.45			0.11		
Verify Score		0.42	0.01	0.47					0.73					0.00			0.29		
PSI- BLAST		2.6e-10	1.2e-07	1.3e-21					5.2e-22					1.2e-20			1.3e-12		•
End		1861	1862	1865					1865					1865			1864		
Start AA		1765	1765	1765					1765					1761			1739		
Chain ID		V		Ą					Ą					A					
PDB ID		1btk	1btn	1fao					1fb8					1fgy	3		1pms		
S B S		179	179	179					179					179			179		

PDB annotation	OXIDOREDUCTASE BETA- PROPELLER, SUPERBARREL, COMPLEX WITH THE COFACTOR PQQ 2 AND THE INHIBITOR METHYLHYDRAZINE, OXIDOREDUCTASE	OXIDOREDUCTASE PDZ DOMAIN, NNOS, NITRIC OXIDE SYNTHASE	PEPTIDE RECOGNITION PEPTIDE RECOGNITION, PROTEIN LOCALIZATION	CYTOKINE LCF, CYTOKINE, LYMPHOCYTE CHEMOATTRACTANT FACTOR, PDZ DOMAIN	KINASE HCASK, GLGF REPEAT, DHR; PDZ DOMAIN, NEUREXIN, SYNDECAN, RECEPTOR CLUSTERING, KINASE	KINASE HCASK, GLGF REPEAT, DHR; PDZ DOMAIN, NEUREXIN, SYNDECAN, RECEPTOR CLUSTERING, KINASE	SIGNAL TRANSDUCTION HDLG, DHR3 DOMAIN; SIGNAL TRANSDUCTION, SH3 DOMAIN, REPEAT	OXIDOREDUCTASE BETA-FINGER
Coumpound	SOLUBLE QUINOPROTEIN GLUCOSE DEHYDROGENASE; CHAIN: A, B;	NEURONAL NITRIC OXIDE SYNTHASE; CHAIN: A; HEPTAPEPTIDE; CHAIN: B;	PSD-95; CHAIN: A; CRIPT; CHAIN: B;	INTERLEUKIN 16; CHAIN: NULL;	HCASK/LIN-2 PROTEIN; CHAIN: A, B;	HCASK/LIN-2 PROTEIN; CHAIN: A, B;	HUMAN DISCS LARGE PROTEIN; CHAIN: NULL;	NEURONAL NITRIC OXIDE SYNTHASE
SeqFold Score								
PMF Score	0.93	0.59	1.00	0.78	0.63	0.77	1.00	0.86
Verify Score	0.25	-0.11	0.73	0.34	-0.10	0.05	0.48	0:30
PSI- BLAST	1e-69	8.5e-13	8.5e-20	6.8e-14	1.7e-09	le-11	1.5e-19	8.5e-13
End AA	447	102	77	71	77	73	16	102
Start AA	115	5	2	2	1	2	2	5
Chain D	A	¥	A		A	¥		V
PDB TD	loru	1b8q	1be9	1i16	lkwa	lkwa	1pdr	lqau
SEQ NO EQ	180	181	181	181	181	181	181	181

PDB annotation		MEMBRANE PROTBIN/OXIDOREDUCTASE BETA- FINGER, HETERODIMER	PEPTIDE RECOGNITION PSD-95; PDZ DOMAIN, NEURONAL NITRIC OXIDE SYNTHASE, NMDA RECEPTOR 2 BINDING	HYDROLASE PDZ DOMAIN, HUMAN PHOSPHATASE, HPTP1E, PTP-BAS, SPECIFICITY 2 OF BINDING	G PROTEIN G PROTEIN, RAS, ARF, ARF6, MEMBRANE TRAFFIC	SIGNALING PROTEIN ARF-LIKE PROTEIN 3, ARL3; PROTEIN-GDP COMPLEX WITHOUT MAGNESIUM, ARF FAMILY, RAS 2 SUPERFAMILY, G-DOMAIN	PROTEIN TRANSPORT GDP- BINDING, MEMBRANE TRAFFICKIN, NON-MYRISTOYLATED 1HUR 16	PROTEIN TRANSPORT GDP- BINDING, MEMBRANE TRAFFICKIN,
Coumpound	(RESIDUES 1-130); CHAIN: A;	ALPHA-1 SYNTROPHIN (RESIDUES 77-171); CHAIN: A; NEURONAL NITRIC OXIDE SYNTHASE (RESIDUES 1-130); CHAIN: B:	POSTSYNAPTIC DENSITY PROTEIN 95; CHAIN: A;	TYROSINE PHOSPHATASE (PTP- BAS, TYPE 1); CHAIN: A;	ADP- RIBOSYLATION FACTOR 6; CHAIN: A;	ADP- RIBOSYLATION FACTOR-LIKE PROTEIN 3; CHAIN: A;	HUMAN ADP- RIBOSYLATION FACTOR 1; 1HUR 5 CHAIN: A, B; 1HUR 7	HUMAN ADP. RIBOSYLATION
SeqFold Score								178.06
PMF Score		86:0	1.00	1.00	1.00	1.00	1.00	
Verify Score		0.59	0.48	0.77	0.94	0.95	0.95	
PSI- BLAST		16-18	1.2e-21	1.7e-18	3.4e-60	8.5e-51	8.5e-66	8.5e-66
End		48	08	77	177	176	771	179
Start AA		2	4	2	∞	4	2	2
Chain ID		A	Ą	Ą	Ą	¥	A	Y
PDB ID		lqav	1qic	3pdz	1e0s	lfzq	1hur	1hur
SEQ NO:		181	181	181	182	182	182	182

		I	I				T -					7								Т-			
PDB annotation	NON-MYRISTOYLATED 1HUR 16						COMPLEX (BLOOD COAGULATION/INHIBITIOR)	AUTOPROTHROMBIN IIA;	PROTEINASE), PLASMA CALCIUM	BINDING, 2 GLYCOPROTEIN,	COMPLEX (BLOOD COAGULATION/INHIBITOR)	BLOOD COAGULATION, SERINE	PROTEASE, COMPLEX, CO-FACTOR,	2 RECEPTOR ENZYME, INHIBITOR,	PROTEASE/COFACTOR/LIGAND)					BLOOD COAGULATION, SERINE	PROTEASE, COMPLEX, CO-FACTOR,	Z KECEFIOK ENZYME, INHIBITOK, GI.A EGF 3 COMPLEX (SERINF	PROTEASE/COFACTOR/LIGAND)
Coumpound	FACTOR 1; 1HUR 5 CHAIN: A, B; 1HUR 7		PROTEINASE INHIBITOR(TRYPSIN) TRYPSIN	IATA 3 (NMR,	MINIMIZED AVERAGE STRIICTURE) 14TA	4	ACTIVATED PROTEIN C: CHAIN:	C, L; D-PHE-PRO-	inter, Circuit, 1,			ВГООД	COAGULATION	FACTOR VIIA;	CHAIN: L, H; SOLUBLE TISSUE	FACTOR; CHAIN: T,	U; D-PHE-PHE-ARG-	CHLOROMETHYLKE	TONE (DFFRCMK) WITH CHAIN: C;	вгоор	COAGULATION	CHAIN: L. H:	SOLUBLE TISSUE
SeqFold Score																							
PMF Score			0.09				-0.19					-0.18								-0.15			
Verify Score			0.29			_	0.29				,	0.49								80.0			
PSI- BLAST			5.2e-12				5.1e-11					1.7e-10								3.4e-12	-		
End AA			968				940					868								943			
Start AA			834	· · · · · · · · · · · · · · · · · · ·			845					819								851			
Chain ID							1					1								L			
PDB TD			lata				laut					1dan								ldan			
SEQ NO:			183				183					183								183			

PDB annotation		BLOOD COAGULATION, SERINE PROTEASE, COMPLEX, CO-FACTOR, 2 RECEPTOR ENZYME, INHIBITOR, GLA, EGF, 3 COMPLEX (SERINE PROTEASE/COFACTOR/LIGAND)	HYDROLASE/HYDROLASE NHIBITOR PROTEIN-PEPTIDE COMPLEX	HYDROLASE/HYDROLASE INHIBITOR PROTEIN-PEPTIDE COMPLEX	HYDROLASE/HYDROLASE INHIBITOR PROTEIN-PEPTIDE
Coumpound	FACTOR; CHAIN: T, U; D-PHE-PHE-ARG- CHLOROMETHYLKE TONB (DFFRCMK) WITH CHAIN: C;	BLOOD COAGULATION FACTOR VIIA; CHAIN: L, H; SOLUBLE TISSUE FACTOR; CHAIN: T, U; D-PHE-PHE-ARG- CHLOROMETHYLKE TONE (DFFRCMK) WITH CHAIN: C;	DES-GLA FACTOR VIIA (HEA VY CHAIN); CHAIN: H, I; DES-GLA FACTOR VIIA (LIGHT CHAIN); CHAIN: L, M; (DPN)- PHE-ARG; CHAIN: C, D; PEPTIDE E-76; CHAIN: X, Y;	DES-GLA FACTOR VIIA (HEAVY CHAIN); CHAIN: H, I; DES-GLA FACTOR VIIA (LIGHT CHAIN); CHAIN: L, M; (DPN)- PHE-ARG; CHAIN: C, D; PEPTIDE B-76; CHAIN: X, Y;	DES-GLA FACTOR VIIA (HEAVY
SeqFold Score					
PMF Score		-0.18	-0.18	-0.12	-0.14
Verify Score		0.0	0.20	0.65	0.30
PSI- BLAST		1.7e-10	8.5e-14	1.7e-10	3.4e-12
End AA		1020	427	868	943
Start		939	330	819	851
Chain ID		H	L	-	1
PDB UD		1dan	1dva	ldva	1dva
SEQ EN CR		183	183	183	183

PDB annotation	COMPLEX	SERINE PROTEINASE COAGULATION FACTOR II; COAGULATION FACTOR II; FETOMODULIN, TM, CD141 ANTIGEN; EGR-CMK SERINE PROTEINASE, EGF-LIKE DOMAINS, ANTICOAGULANT COMPLEX, 2 ANTIFIBRINOLYTIC COMPLEX	SERINE PROTEINASE COAGULATION FACTOR II; COAGULATION FACTOR II; FETOMODULIN, TM, CD141 ANTIGEN; EGR-CMK SERINE PROTEINASE, EGF-LIKE DOMAINS, ANTICOAGULANT COMPLEX, 2 ANTIFIBRINOLYTIC COMPLEX	BLOOD CLOTTING COMPLEX(SERINE PROTEASE/COFACTOR/LIGAND), BLOOD COAGULATION, 2 SERINE PROTEASE, COMPLEX, CO-FACTOR, RECEPTOR ENZYME, 3 INHIBITOR,
Coumpound	CHAIN); CHAIN: H, I; DES-GLA FACTOR VIIA (LIGHT CHAIN); CHAIN: L, M; (DPN)- PHE-ARG; CHAIN: C, D; PEPTIDE B-76; CHAIN: X, Y;	THROMBIN LIGHT CHAIN; CHAIN: A, B, C, D; THROMBIN HEAVY CHAIN; CHAIN: M, N, O, P; THROMBOMODULI N; CHAIN: I, J, K, L; THROMBIN INHIBITOR L-GLU-L- GLY-L-ARM; CHAIN: E, F, G, H;	THROMBIN LIGHT CHAIN; CHAIN: A, B, C, D; THROMBIN HEAVY CHAIN; CHAIN: M, N, O, P; THROMBOMODULI N; CHAIN: I, I, K, L; THROMBIN INHIBITOR L-GLU-L- GLY-L-ARM; CHAIN: E, F, G, H;	BLOOD COAGULATION FACTOR VIIA; CHAIN: L; BLOOD COAGULATION FACTOR VIIA;
SeqFold Score				
PMF Score		-0.20	-0.20	-0.18
Verify Score		0.02	0.02	0.27
PSI- BLAST		3.4e-11	3.4e-11	1.7e-10
End AA		1294	1294	868
Start AA		1167	1167	819
Chain ID		.	п	J
PDB CD		1dx5	1dx5	1fak
SEQ NO:		183	183	183

PDB annotation	GLA, EGF, COMPLEX (SERINE 4 PROTEASE/COFACTOR/LIGAND), BLOOD CLOTTING	BLOOD CLOTTING COMPLEX(SERINE PROTEASE/COFACTOR/LIGAND), BLOOD COAGULATION, 2 SERINE PROTEASE, COMPLEX, CO-FACTOR, RECEPTOR ENZYME, 3 INHIBITOR, GLA, EGF, COMPLEX (SERINE 4 PROTEASE/COFACTOR/LIGAND), BLOOD CLOTTING	BLOOD CLOTTING COMPLEX(SERINE PROTEASE/COFACTOR/LIGAND), BLOOD COAGULATION, 2 SERINE PROTEASE, COMPLEX, CO-FACTOR, RECEPTOR ENZYME, 3 INHIBITOR, GLA, EGF, COMPLEX (SERINE 4 PROTEASE/COFACTOR/LIGAND), BLOOD CLOTTING	BLOOD CLOTTING COMPLEX(SERINE PROTEASE/COFACTOR/LIGAND), BLOOD COAGULATION, 2 SERINE PROTEASE, COMPLEX, CO-FACTOR, RECEPTOR ENZYME, 3 INHIBITOR, GLA, EGF, COMPLEX (SERINE 4 PROTEASE/COFACTOR/LIGAND), BLOOD CLOTTING	GLYCOPROTEIN GLYCOPROTEIN
Coumpound	CHAIN: H; SOLUBLE TISSUB FACTOR; CHAIN: T; SL15; CHAIN: I;	BLOOD COAGULATION FACTOR VIIA; CHAIN: L; BLOOD COAGULATION FACTOR VIIA; CHAIN: H; SOLUBLE TISSUE FACTOR; CHAIN: T; 5L15; CHAIN: I;	BLOOD COAGULATION FACTOR VIIA; CHAIN: L; BLOOD COAGULATION FACTOR VIIA; CHAIN: H; SOLUBLE TISSUE FACTOR; CHAIN: T; 5L15;	BLOOD COAGULATION FACTOR VIIA; CHAIN: L; BLOOD COAGULATION FACTOR VIIA; CHAIN: H; SOLUBLE TISSUE FACTOR; CHAIN: T; 5L15; CHAIN: I;	LAMININ; CHAIN:
SeqFold Score					
PMF Score		-0.18	-0.14	-0.15	-0.15
Verify Score		0.27	0.05	0.10	0.21
PSI- BLAST	·	1.7e-10	3.46-12	3.46-12	1e-09
End		868	943	943	472
Start		819	851	851	333
Chain ID		ы	1	ıı	
PDB ID		1fak	1fak	Ifak	1160
SEQ FIGURE		183	183	183	183

	T			٠,		Γ			 r		<u> </u>							
PDB annotation		GLYCOPROTEIN GLYCOPROTEIN	GLYCOPROTEIN GLYCOPROTEIN	COMPLEX (BLOOD COAGULATION/INHIBITOR) CHRISTMAS FACTOR; COMPLEX, INHIBITOR, HEMOPHILIA/EGF, BLOOD COAGULATION, 2 PLASMA,	SERVICE TROJEASE, CALCIUM- BINDING, HYDROLASE, 3 GLYCOPROTEIN	COMPLEX (BLOOD	COAGULATION/INHIBITOR) CHRISTMAS FACTOR; COMPLEX,	INHIBITOR, HEMOPHILIA/EGF, BLOOD COAGULATION, 2 PLASMA.	SERINE PROTEASE, CALCIUM-	BINDING, HYDROLASE, 3 GLYCOPROTEIN	COMPLEX (BLOOD	COAGULATION/INHIBITOR) CHRISTMAS FACTOR; COMPLEX,	INHIBITOR, HEMOPHILIA/EGE,	SERINE PROTEASE, CALCIUM.	BINDING, HYDROLASE, 3	SERINE PROTEASE FVIIA; FVIIA;	BLOOD COAGULATION, SERINE PROTEASE	
Coumpound	NULL;	LAMININ; CHAIN: NULL;	LAMININ; CHAIN: NULL;	FACTOR IXA; CHAIN: C, L.; D-PHE- PRO-ARG; CHAIN: I;		FACTOR IXA;	CHAIN: C, L.; D-PHE- PRO-ARG; CHAIN: I;				FACTOR IXA;	CHAIN: C, L.; D-PHE- PRO-ARG; CHAIN: I;				COAGULATION	FACTOR VIIA (LIGHT CHAIN);	CHAIN-L;
SeqFold Score													-					
PMF Score		-0.18	-0.18	-0.14		-0.18	-				-0.19	-				-0.19		
Verify Score		0.20	0.20	0.15		0.03					0.09					0.16		
PSI- BLAST		3.4e-15	3.4e-15	1.4e-10		2.6e-08					1.7e-09					5.1e-11		
End AA		902	902	438		920					868					1339		
Start AA		755	755	330		772					819					1263		
Chain ID				H		L							_	_		1		
PDB CD		1klo	1klo	Pfx		1pfx				_	lpfx -			-		1qfk		
SEQ NO IS		183	183	183		183										183		

PDB annotation		SERINE PROTEASE FVIIA; BLOOD COAGULATION, SERINE PROTEASE	SERINE PROTEASE FVIIA; FVIIA; BLOOD COAGULATION, SERINE PROTEASE	MEMBRANE ADHESION SHORT CONSENSUS REPEAT, SUSHI, COMPLEMENT CONTROL PROTEIN, 2 N-GLYCOSYLATION, MULTI- DOMAIN, MEMBRANE ADHESION	BLOOD COAGULATION FACTOR STUART FACTOR; BLOOD
Coumpound	FACTOR VIIA (HEAVY CHAIN); CHAIN: H; TRIPEPTIDYL INHIBITOR; CHAIN: C;	COAGULATION FACTOR VIIA (LIGHT CHAIN); CHAIN: L; COAGULATION FACTOR VIIA (HEAVY CHAIN); CHAIN: H; TRIPEPTIDYL INHIBITOR; CHAIN: C;	COAGULATION FACTOR VIIA (LIGHT CHAIN); CHAIN: L; COAGULATION FACTOR VIIA (HEAVY CHAIN); CHAIN: H; TRIPEPTIDYL INHIBITOR; CHAIN: C;	HUMAN BETA2- GLYCOPROTEIN I; CHAIN: A;	BLOOD COAGULATION
SeqFold Score					
PMF Score		-0.18	-0.18	-0.15	-0.07
Verify Score		0.32	0.31	0.20	0.22
PSI- BLAST		5.1e-13	6.8e-10	3.9e-08	3.4e-10
End		427	868	488	427
Start AA		334	822	379	334
Chain TD		i i	ъ.	¥	נו
80g E		1qfk	1qfk	1qub	1xka
S B S		183	183	183	183

PDB annotation	COAGULATION FACTOR, SERINE PROTEINASE, EPIDERMAL 2 GROWTH FACTOR LIKE DOMAIN	BLOOD COAGULATION FACTOR STUART FACTOR; BLOOD COAGULATION FACTOR, SERINE PROTEINASE, EPIDERMAL 2 GROWTH FACTOR I IN DOMAIN	BLOOD COAGULATION FACTOR STUART FACTOR; BLOOD COAGULATION FACTOR, SERINE PROTEINASE, EPIDERMAL 2 GROWTH FACTOR LIKE DOMAIN				
Coumpound	FACTOR XA; CHAIN: L, C,	BLOOD COAGULATION FACTOR XA; CHAIN: L, C;	BLOOD COAGULATION FACTOR XA; CHAIN: L, C;	LECTIN (AGGLUTININ) WHEAT GERM AGGLUTININ (ISOLECTIN 2) 9WGA 3	LECTIN (AGGLUTININ) WHEAT GERM AGGLUTININ (ISOLECTIN 2) 9WGA 3	LECTIN (AGGLUTININ) WHEAT GERM AGGLUTININ (ISOLECTIN 2) 9WGA 3	LECTIN (AGGLUTININ) WHEAT GBRM
SeqFold Score							
PMF Score		-0.13	-0.19	-0.19	-0.19	-0.19	-0.19
Verify Score		0.22	0.11	0.02	0.02	0.08	0.08
PSI- BLAST		le-10	3.4e-09	5.1e-11	5.1e-11	5.1e-14	5.1e-14
End		868	940	1364	1364	420	420
Start AA		822	855	1219	1219	277	277
Chain D		7	ы	∢	¥	¥	A
PDB ID		lxka	1xka	9wga	9wga	9wga	9wga
SEQ NO.		183	183	183	183	183	183

PDB annotation																									
Coumpound	AGGLUTININ (ISOLECTIN 2) 9WGA 3	LECTIN (AGGLUTININ)	WHEAT GERM AGGLUTININ	(ISOLECTIN 2) 9WGA 3	LECTIN	(AGGLUTININ)	AGGLUTININ	(ISOLECTIN 2)	9WGA 3	LECTINA IN IN	(AGGLUTININ) WHEAT GERM	AGGLUTININ	(ISOLECTIN 2)	IRCTIN	CAGGITHMEN	WHEAT GERM	AGGLUTININ	(ISOLECTIN 2)	9WGA 3	LECTIN	(AGGLUTININ)	WHEAT GERM	AGGLUTININ	(ISOLECTIN 2) 9WGA 3	LECTIN
SeqFold Score																									
PMF Score		-0.18			-0.18				0.17		-			-0.17						-0.12					-0.12
Verify Score		0.31	•		0.31				0.13					0 13	C1.5					0.29					0.29
PSI- BLAST		1.5e-11			1.5e-11			-	2.40.17	3.45-12			,	3 46-12	21-01-0	-				5.1e-13	_				5.1e-13
. End AA		544			544				200	ì				200						5/6					975
Start AA		318			318				LSL	<u>`</u>				757	3					111				_	777
Chain 10		A			Ą		-		٧	<				A	₹					_ ¥					V
PDB TD		9wga			9wga				0,11,00	2 w ga				Qw03	191					8m6					9wga
S a Š		183			183				183	2				183	3					183					183

PDB annotation				GLYCOSIDASE CGTASE; 1CIU 8 THERMOSTABLE 1CIU 14	GLYCOSDASE CGTASE; 1CIU 8 THERMOSTABLE 1CIU 14
Coumpound	(AGGLUTININ) WHEAT GERM AGGLUTININ (ISOLECTIN 2) 9WGA 3	COAGULATION FACTOR EGF-LIKE MODULE OF BLOOD COAGULATION FACTOR X (N- TERMINAL, IAPO 3 APO FORM) (NMR, 13 STRUCTURES) 1APO 4	COAGULATION FACTOR EGF-LIKE MODULE OF BLOOD COAGULATION FACTOR X (N- TERMINAL, 1APO 3 APO FORM) (NMR, 13 STRUCTURES) 1APO 4	CYCLODEXTRIN GLYCOSYLTRANSF ERASE; ICIU 6 CHAIN: NULL; ICIU	CYCLODEXTRIN GLYCOSYLTRANSF ERASE; ICIU 6 CHAIN: NULL; ICIU
SeqFold Score	,				
PMF Score		0.53	0.53	-0.19	-0.19
Verify Score		0.37	0.37	0.05	0.05
PSI- BLAST		1.3e-06	1.3e-06	5.26-34	5.2e-34
End		1245	1245	385	385
Start AA		1210	1210	39	39
Chain ID					
PDB TD		lapo	lapo	lciu	1ciu
SEQ NG:		184	184	184	184

PDB annotation	GLYCOSIDASE CGTASE; 1CIU 8 THERMOSTABLE 1CIU 14	GLYCOSIDASE CGTASE; 1CIU 8 THERMOSTABLE 1CIU 14	STRUCTURAL PROTEIN INTEGRIN- BINDING PROTEIN, INV GENE	STRUCTURAL PROTEIN INTEGRIN- BINDING PROTEIN, INV GENE				
Coumpound	CYCLODEXTRIN GLYCOSYLTRANSF ERASE, ICIU 6 CHAIN: NULL, ICIU	CYCLODEXTRIN GLYCOSYLTRANSF ERASE; ICIU 6 CHAIN: NULL; ICIU	CYCLODEXTRIN GLYCOSYLTRANSF ERASE; 1CIU 6 CHAIN: NULL; 1CIU	CYCLODEXTRIN GLYCOSYLTRANSF ERASE; 1CIU 6 CHAIN: NULL; 1CIU	CYCLODEXTRIN GLYCOSYLTRANSF ERASE; 1CIU 6 CHAIN: NULL; 1CIU	CYCLODEXTRIN GLYCOSYLTRANSF ERASE; ICIU 6 CHAIN: NULL; ICIU	INVASIN; CHAIN: A;	INVASIN; CHAIN: A;
SeqFold Score								
PMF Score	-0.18	-0.18	-0.19	-0.19	-0.15	-0.15	-0.20	-0.20
Verify Score	0.01	0.01	0.05	0.05	0.03	0.03	0.05	0.05
PSI- BLAST	1.3e-32	1.3e-32	1.3e-26	1.3e-26	3.9e-22	3.9e-22	9.1e-60	9.1e-60
End AA	783	783	1044	1044	1177	1177	749	749
Start AA	404	404	699	699	863	863	264	264
Chain TO							¥	A
PDB ED	1ciu	lciu	lciu	1ciu	lciu	lciu	lcwv	lcwv
SEQ NO.	184	184	184	184	184	184	184	184

PDB annotation	STRUCTURAL PROTEIN INTEGRIN- BINDING PROTEIN, INV GENE	STRUCTURAL PROTEIN INTEGRIN- BINDING PROTEIN, INV GENE	STRUCTURAL PROTEIN INTEGRIN- BINDING PROTEIN, INV GENE	STRUCTURAL PROTEIN INTEGRIN- BINDING PROTEIN. INV GENE	BLOOD COAGULATION, SERINE PROTEASE, COMPLEX, CO-FACTOR.	2 RECEPTOR ENZYME, INHIBITOR,	GLA, EGF, 3 COMPLEX (SERINE PROTEASE/COFACTOR/LIGAND)				BLOOD COAGULATION. SERINE	PROTEASE, COMPLEX, CO-FACTOR, 2 RECEPTOR ENZYME, INHIBITOR	GLA, EGF, 3 COMPLEX (SERINE	PROTEASE/COFACTOR/LIGAND)					COAGULATION FACTOR CRYSTAL	SIRUCIUKE, EPIDERMAL GROWTH	FACTOR, EGF, 2 CALCIOM- BINDING, EGF-LIKE DOMAIN.	STRUCTURE AND FUNCTION, 3 HUMAN FACTOR IX,
Coumpound	INVASIN; CHAIN: A;	INVASIN; CHAIN: A;	INVASIN; CHAIN: A;	INVASIN; CHAIN: A;	BLOOD COAGULATION	FACTOR VIIA;	CHAIN: L, H; SOLUBLE TISSUE	FACTOR; CHAIN: T,	U; D-PHE-PHE-ARG- CHLOROMETHYLKE	TONE (DFFRCMK) WITH CHAIN: C:	BLOOD	COAGULATION FACTOR VIIA:	CHAIN: L, H;	SOLUBLE TISSUE	FACTOR; CHAIN: I,	CHI OROMETHYLKE	TONE (DFFRCMK)	WITH CHAIN: C;	FACTOR IX; CHAIN:	پر ر:		
SeqFold Score	101.45	101.45				-	-															
PMF Score			-0.19	-0.19	0.04						0.04							,	0.76			
Verify Score			0.04	0.04	0.15			-			0.15								0.32		•	
PSI- BLAST	1.2e-61	1.2e-61	1e-56	1e-56	8.5e-10						8.5e-10							10	2.Ie-0/			
End AA	966	966	1082	1082	1282						1282		····					27.01	7571		-	·
Start AA	521	521	561	261	1210						1210							0101	1210			
Chain D	A	A	А	A	ب ا						r						<u> </u>	-	q			
PDB ID	lcwv	1cwv	lcwv	lcwv	ldan						ldan	1.							H H H H H H H H H H H H H H H H H H H			
SEQ NO:	184	184	184	184	184						184							5	+01			

	_									_			_									
PDB annotation	COAGULATION FACTOR	COAGULATION FACTOR CRYSTAL STRUCTURE, BPIDERMAL GROWTH FACTOR, EGF, 2 CALCIUM-	BINDING, EGF-LIKE DOMAIN, STRUCTURE AND FUNCTION, 3	HUMAN FACTOR IX, COAGULATION FACTOR	BLOOD CLOTTING COMPLEX(SERINE	PROTEASE/COFACTOR/LIGAND), BLOOD COAGULATION, 2 SERINE	PROTEASE, COMPLEX, CO-FACTOR, RECEPTOR BNZYME, 3 INHIBITOR,	GLA, EGF, COMPLEX (SERINE 4	PROTEASE/COFACTOR/LIGAND), BLOOD CLOTTING	BLOOD CLOTTING	COMPLEX(SERINE	PROTEASE/COFACTOR/LIGAND),	BLOOD COAGULATION, 2 SERINE	PROTEASE, COMPLEX, CO-FACTOR, PECEDITOP SINISTING	GLA FGF COMPLEX (SERINE 4	PROTEASE/COFACTOR/LIGAND),	BLOOD CLOTTING		COMPLEX (BLOOD COAGULATION/INHIBITOR)	CHRISTINGS FACTOR, COMPLETA, INHIBITOR HEMOPHII IA/FIGE	BLOOD COAGULATION, 2 PLASMA,	SERINE PROTEASE, CALCIUM- BINDING, HYDROLASE, 3
Coumpound		FACTOR IX; CHAIN: B, C;			BLOOD COAGULATION	FACTOR VIIA; CHAIN: L; BLOOD	COAGULATION FACTOR VIIA:	CHAIN: H; SOLUBLE	TISSUE FACTOR; CHAIN: T; 5L15; CHAIN: I.	BLOOD	COAGULATION	FACTOR VIIA;	CHAIN: L; BLOOD	COAGULATION	CHAIN H. SOLIBLE	TISSUE FACTOR;	CHAIN: T; 5L15;	CHAIN: I;	FACTOR IXA; CHAIN: C, L,; D-PHE-	FRO-ARG; CHAIN; I;		
SeqFold Score																						
PMF		0.76		-	0.00					000	2								-0.11			
Verify Score		0.32			-0.03					-0.03	3								0.04			
PSI- BLAST		5.1e-07			8.5e-10					8 5e-10	21.5							;	5.2e-10			
End AA		1242		•	1282					1282	7071								1242			
Start AA		1210			1210					1210	0171								1189			
Chain ID		B			1						۱								7			
PDB DD		1edm			1fak					1651	IIak								lpfx			
SEQ EQ EQ		184			184					107	†o1								184			

	T					T											Т							
PDB annotation	GLYCOPROTEIN	COMPLEX (BLOOD COAGULATION/INHIBITOR)	CHRISTMAS FACTOR; COMPLEX, INHIBITOR, HEMOPHILIA/EGF,	BLOOD COAGULATION, 2 PLASMA, SERINE PROTEASE, CALCITM.	BINDING, HYDROLASE, 3 GLYCOPROTEIN	COMPLEX (BLOOD	COAGOLA HON/INHIBITOR) CHRISTMAS FACTOR; COMPLEX,	INHIBITOR, HEMOPHILIA/EGF,	BLOOD COAGULATION, 2 PLASMA, SHENNE BROTEASE CATOURY	BINDING, HYDROLASE, 3	COMPLEX (RI OOD	COAGULATION/INHIBITOR) CHRISTMAS FACTOR: COMMITES	INHIBITOR, HEMOPHILIA/FGF	BLOOD COAGULATION, 2 PLASMA.	SERINE PROTEASE, CALCIUM-	BINDING, HYDROLASE, 3 GLYCOPROTEIN	SERINE PROTEASE FVIIA; FVIIA;	BLOOD COAGULATION, SERINE	PROTEASE					
Coumpound		FACTOR IXA; CHAIN: C, L.; D-PHE-	FRO-ARG; CHAIN: I;			FACTOR IXA;	PRO-ARG; CHAIN: I;				FACTOR IXA:	CHAIN: C, L.; D-PHE-PRO-ARG: CHAIN: I:	(1) (2) (2) (2) (3) (3) (4) (4) (4) (4) (4) (4) (4) (4) (4) (4				COAGULATION	FACTOR VIIA	(LIGHT CHAIN); CHAIN: L:	COAGULATION	FACTOR VIIA	(HEAVY CHAIN);	CHAIN: H;	INHIBITOR; CHAIN:
SeqFold Score															···									
PMF Score		-0.11				0.11					0.11						-0.13							
Verify Score		0.04				0.15					0.15						0.04							
PSI- BLAST		5.2e-10				1e-08		•			le-08				•		3.4e-09							
End AA		1242				1273	-				1273						1282							
Start AA		1189				1210					1210				-		1214	•						
Chain ID		บ				L)					L									•				
PDB ID		1pfx	-,,,,			1pfx					1pfx		- ,_	_			Jqfk 							
SEQ NO:		184	<u>.</u>			184					184						184							

PDB annotation		SERINE PROTEASE FVIIA; FVIIA; BLOOD COAGULATION, SERINE PROTEASE	PLASMINOGEN ACTIVATION	PLASMINOGEN ACTIVATION	PLASMINOGEN ACTIVATION	PLASMINOGEN ACTIVATION	GLYCOPROTEIN GLYCOPROTEIN, HYDROLASE, SERINE PROTEASE, PLASMA, BLOOD 2 COAGULATION FACTOR	GLYCOPROTEIN GLYCOPROTEIN, HYDROLASE, SERINE PROTEASE,
Coumpound	c;	COAGULATION FACTOR VIIA (LIGHT CHAIN); CHAIN: L; COAGULATION FACTOR VIIA (HEAVY CHAIN); CHAIN: H; TRIPEPTIDYL INHIBITOR; CHAIN:	T-PLASMINOGEN ACTIVATOR F1-G; ITPG 7 CHAIN: NULL; ITPG 8	T-PLASMINOGEN ACTIVATOR F1-G; ITPG 7 CHAIN: NULL; ITPG 8	T-PLASMINOGEN ACTIVATOR F1-G; 1TPG 7 CHAIN: NULL; 1TPG 8	T-PLASMINOGEN ACTIVATOR F1-G; ITPG 7 CHAIN: NULL; ITPG 8	COAGULATION FACTOR X; CHAIN: NULL;	COAGULATION FACTOR X; CHAIN:
SeqFold Score								
PMF Score		-0.13	0.07	0.07	0.03	0.03	-0.14	-0.14
Verify Score		0.04	0.44	0.44	-0.12	-0.12	0.29	0.29
PSI- BLAST		3.4e-09	2.6e-10	2.6e-10	1.7e-07	1.7e-07	3.9e-10	3.9e-10
End AA		1282	1242	1242	1246	1246	1245	1245
Start AA		1214	1189	1189	1197	1197	1189	1189
Chain								
PDB TD		1qfk	1tpg	1tpg	1tpg	1tpg	lwhe	lwhe
S B S		184	184	184	184	184	184	184

PDB annotation	PLASMA, BLOOD 2 COAGULATION FACTOR			HYDROLASE PNB ESTERASE; ALPHA-BETA HYDROLASE, DIRECTED EVOLUTION, ORGANIC ACTIVITY, 2 PNB ESTERASE	LIPASE ESTERASE, SUBSTRATE/PRODUCT-BOUND ICLE 9	HYDROLASE (SERINE ESTERASE) HYDROLASE (SERINE ESTERASE), HYDROLASE, SERINE ESTERASE, 2 SYNAPSE, MEMBRANE, NERVE, MUSCLE, SIGNAL, NEUROTRANSMITTER 3 DEGRADATION, GLYCOPROTEIN, GPI-ANCHOR, ALTERNATIVE	SFLICING CHOLINESTERASE SERINE HYDROLASE, NEUROTRANSMITTER CLEAVAGE,
Coumpound	NULL;	LECTIN (AGGLUTININ) WHEAT GERM AGGLUTININ (ISOLECTIN 2) 9WGA 3	LECTIN (AGGLUTININ) WHEAT GERM AGGLUTININ (ISOLECTIN 2) 9WGA 3	PARA- NITROBENZYL ESTERASE; CHAIN: A;	CHOLESTEROL ESTERASE; ICLE 4 CHAIN: A, B; ICLE 5	ACETYLCHOLINEST ERASE; CHAIN: A;	ACETYLCHOLINEST ERASE; CHAIN: A;
SeqFold Score							
PMR Score		-0.19	-0.19	0.40	0.33	0.10	0.54
Verify Score		0.22	0.22	-0.84	-0.66	-0.91	-0.42
PSI- BLAST		5.1e-08	5.1e-08	3.4e-29	1.5e-23	1.7e-24	3.4e-30
End AA		1293	1293	83	83	8	83
Start AA		1191	1191	1		-	1
Chain ID		¥	¥	A	A	· V	4
PDB ID		9wga	9wga	1c7j	1cle	1dx4	lea5
S E S		184	184	.185	185	185	185

PDB annotation	CATALYTIC 2 TRIAD, ALPHA/BETA HYDROLASE	HYDROLASE BILE SALT ACTIVATED LIPASE, ESTERASE, CATALYTIC DOMAIN		HYDROLASE MACHE, HYDROLASE, SERINE ESTERASE, ACETYLCHOLINESTERASE, TETRAMER, 2 HYDROLASE FOLD, GLYCOSYLATED PROTEIN	HYDROLASE PNB ESTERASE; ALPHA-BETA HYDROLASE DIRECTED EVOLUTION		HYDROLASE BILE SALT ACTIVATED LIPASE, BILE SALT STIMULATED HYDROLASE, SERINE ESTERASE, LIPASE	
Coumpound		BILE SALT ACTIVATED LIPASE; CHAIN: A;	HYDROLASE LIPASE (B.C.3.1.1.3) (TRIACYLGLYCERO L LIPASE) COMPLEXED WITH 1LPP 3 HEXADECANESULF ONATE 1LPP 4 1LPP	ACETYLCHOLINEST ERASE; CHAIN: A, B, C, D;	PARA- NITROBENZYL ESTERASE; CHAIN: A;	HYDROLASE(CARB OXYLIC ESTERASE) LIPASE (E.C.3.1.1.3) TRIACYLGLYCEROL HYDROLASE 1THG 3	CHOLESTEROL ESTERASE; CHAIN: NULL;	METALLOTHIONEIN
SeqFold Score				_				
PMF Score		0.25	0.16	0.75	0.48	0.19	0.36	0.77
Verify Score		-0.93	-0.93	-0.76	-0.51	-0.65	-0.93	-0.83
PSI- BLAST		5.1e-32	8.5e-23	1.7e-29	1.7e-29	1.5e-25	3.4e-32	0.0052
End		83	8	83	83	83	83	165
Start				2		-	1	132
Chain ID		A		V	¥			
FDB ED		1f6w	11pp	1maa	1qe3	1thg	2bce	1mt
S B S		185	185	185	185	185	185	186

PDB annotation		
Coumpound	CD-7 METALLOTHIONEIN -2 (ALPHA DOMAIN) (NMR\$) IMRTA 2	
SeqFold Score		
PMF Score		
Verify Score		
PSI- BLAST		
End AA		
Start AA		
Chain		
PDB TD		
S 8 8		

TABLE 6

SEQ ID NO:	Position of Signal Peptide	Maximum score	Mean score
94	1-26	0.988	0.911
95	1-17	0.977	0.921
96	1-32	0.969	0.847
97	1-32	0.969	0.847
98	1-16	0.896	0.833
99	1-19	0.914	0.625
100	1-20	0.888	0.583
101	1-22	0.932	0.756
103	1-18	0.972	0.936
104	1-17	0.979	0.961
105	1-24	0.961	0.807
106	1-29	0.977	0.852
107	1-45	0.971	0.702
108	1-24	0.969	0.898
109	1-34	0.988	0.805
110	1-17	0.984	0.923
114	1-18	0.975	0.958
120	1-17	0.977	0.921
124	1-31	0.985	0.926
126	1-42	0.988	0.594
127	1-19	0.960	0.851
136	1-26	0.981	0.865
137	1-18	0.975	0.958
142	1-17	0.977	0.921
150	1-16	0.896	0.833
156	1-19	0.914	0.625
162	1-16	0.939	0.838
164	1-28	0.961	0.857
167	1-22	0.968	0.875
169	1-25	0.971	0.893
170	1-16	0.948	0.836
172	1-19	0.960	0.851
174	1-30	0.972	0.658
175	1-31	0.965	0.894
176	1-22	0.979	0.697
182	1-15	0.926	0.631
185	1-20	0.952	0.660
186	1-42	0.994	0.973

TABLE 7

SEQ ID NO:	Chromosomal Location
1	22q11
2	5
3	20
4	20
5	20
7	17
10	17
11	19q13.3-q13.4
16	2p21
19	21
20	11q13
21	17
22	1p36.2
23	1p36.2
24	15
25	15
26	7
27	9q21-q22
28	17
31	1
32	13
36	11p15
37	7q22
38	17
40	11q23.3
41	10q25-q26
42	11q13
43	19p13.1
44	19p13.1 17
45	7q32
46	19
47	9q34
49	9q21-q22
50	20q13.3
51	2q35 9
52	
54	9q34
55	9q34
56	17
57	14q32
58	20
60	5
61	16q24.3
62	16q24.3
64	4q34.1-q35.1
65	4q34.1-q35.1
66	9
67	15
68	11
69	14
70	10
71	2cen-q13
72	16
74	4p16.3

SEQ ID NO:	Chromosomal Location
75	13
76	1p36.2
77	4p16-p15
80	1
81	1p35-p31.3
82	1p35-p31.3
86	22q13.33
87	1q41
90	11p15
91	7q22
93	11p15.5

TABLE 8

EQ ID NO: of Full-length Nucleotide Sequence	SEQ ID NO: of Full-length Peptide Sequence	SEQ ID NO: in Priority Application USSN 09/728,952
1	94	2
2	95	3
3	96	4
4	97	5
5	98	6
6	99	7
7	100	12
8	101	13
9	102	14
10	103	15
11	104	16
12	105	17
13	106	18
14	107	19
15	108	20
16	109	22
17	110	23
18	111	24
19	112	26
20	113	27
21	114	28
22	115	
23	116	29
24	117	30
25		31
26	118	32
27	119	33
28	120	34
	121	35
29	122	36
30	123	37
31	124	38
32	125	39
33	126	40
34	127	41
35	128	42
36	129	43
37	130	44
38	131	45
39	132	46
40	133	47
41	134	48
42	135	49
43	136	50
44	137	51
45	138	52
46	139	53
47	140	54
48	141	55
49	142	57
50	143	58
51	144	59

SEQ ID NO: of Full-length	SEQ ID NO: of Full-length	SEQ ID NO: in Priority
Nucleotide Sequence	Peptide Sequence	Application USSN 09/728,952
52	145	60
53	146	61
54	147	62
55	148	63
56	149	64
57	150	65
58	151	66
59	152	67
60	153	68
61	154	69
62	155	70
63	156	71
64	157	72
65	158	73
66	159	74
67	160	75
68	161	76
69	162	77
70	163	78
71	164	79
72	165	80
73	166	81
74	167	82
75	168	83
76	169	84
77	170	85
78	171	86
79	172	87
80	173	88
81	174	89
82	175	90
83	176	91
84	177	92
85	178	93
86	179	94
87	180	95
88	181	96
89	182	97
90	183	98
91	184	99
92	185	100
93	186	101

WHAT IS CLAIMED IS:

1. An isolated polynucleotide comprising a nucleotide sequence selected from the group consisting of SEQ ID NO: 1-93, a mature protein coding portion of SEQ ID NO: 1-93, an active domain coding portion of SEQ ID NO: 1-93, and complementary sequences thereof.

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- 2. An isolated polynucleotide encoding a polypeptide with biological activity, wherein said polynucleotide hybridizes to the polynucleotide of claim 1 under stringent hybridization conditions.
- 10 3. An isolated polynucleotide encoding a polypeptide with biological activity, wherein said polynucleotide has greater than about 90% sequence identity with the polynucleotide of claim 1.
 - 4. The polynucleotide of claim 1 wherein said polynucleotide is DNA.

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- 5. An isolated polynucleotide of claim 1 wherein said polynucleotide comprises the complementary sequences.
- 6. A vector comprising the polynucleotide of claim 1.

- 7. An expression vector comprising the polynucleotide of claim 1.
- 8. A host cell genetically engineered to comprise the polynucleotide of claim 1.
- 9. A host cell genetically engineered to comprise the polynucleotide of claim 1 operatively associated with a regulatory sequence that modulates expression of the polynucleotide in the host cell.
- 10. An isolated polypeptide, wherein the polypeptide is selected from the group consisting 30 of:
 - (a) a polypeptide encoded by any one of the polynucleotides of claim 12
 - (b) a polypeptide encoded by a polynucleotide hybridizing under stringent conditions with any one of SEQ ID NO: 1-93; and

- (c) a polypeptide of any one of SEQ ID NO: 94-186.
- 11. A composition comprising the polypeptide of claim 10 and a carrier.
- 5 12. An antibody directed against the polypeptide of claim 10.
 - 13. A method for detecting the polynucleotide of claim 1 in a sample, comprising:
 - a) contacting the sample with a compound that binds to and forms a complex with the polynucleotide of claim 1 for a period sufficient to form the complex; and
- b) detecting the complex, so that if a complex is detected, the polynucleotide of claim 1 is detected.
 - 14. A method for detecting the polynucleotide of claim 1 in a sample, comprising:
- a) contacting the sample under stringent hybridization conditions with nucleic acid primers that anneal to the polynucleotide of claim 1 under such conditions;
 - b) amplifying a product comprising at least a portion of the polynucleotide of claim 1; and
- c) detecting said product and thereby the polynucleotide of claim 1 in the 20 sample.
 - 15. The method of claim 14, wherein the polynucleotide is an RNA molecule and the method further comprises reverse transcribing an annealed RNA molecule into a cDNA polynucleotide.

- 16. A method for detecting the polypeptide of claim 10 in a sample, comprising:
- a) contacting the sample with a compound that binds to and forms a complex with the polypeptide under conditions and for a period sufficient to form the complex; and
- b) detecting formation of the complex, so that if a complex formation is detected, the polypeptide of claim 10 is detected.

17. A method for identifying a compound that binds to the polypeptide of claim 10, comprising:

- a) contacting the compound with the polypeptide of claim 10 under conditions sufficient to form a polypeptide/compound complex; and
- b) detecting the complex, so that if the polypeptide/compound complex is detected, a compound that binds to the polypeptide of claim 10 is identified.
 - 18. A method for identifying a compound that binds to the polypeptide of claim 10, comprising:
- a) contacting the compound with the polypeptide of claim 10, in a cell, under conditions sufficient to form a polypeptide/compound complex, wherein the complex drives expression of a reporter gene sequence in the cell; and
 - b) detecting the complex by detecting reporter gene sequence expression, so that if the polypeptide/compound complex is detected, a compound that binds to the polypeptide of claim 10 is identified.
 - 19. A method of producing the polypeptide of claim 10, comprising,
 - a) culturing a host cell comprising a polynucleotide sequence selected from SEQ ID NO: 1-93, a mature protein coding portion of SEQ ID NO: 1-93, an active domain coding portion of SEQ ID NO: 1-93, complementary sequences thereof and a polynucleotide sequence hybridizing under stringent conditions to SEQ ID NO: 1-93, under conditions sufficient to express the polypeptide in said cell; and
 - b) isolating the polypeptide from the cell culture or cells of step (a).
- 25 20. An isolated polypeptide comprising an amino acid sequence selected from the group consisting of any one of the polypeptides SEQ ID NO: 94-186, the mature protein portion thereof, or the active domain thereof.
- 21. The polypeptide of claim 20 wherein the polypeptide is provided on a polypeptide 30 array.
 - 22. A collection of polynucleotides, wherein the collection comprising the sequence information of at least one of SEQ ID NO: 1-93.

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23. The collection of claim 22, wherein the collection is provided on a nucleic acid array.

- 24. The collection of claim 23, wherein the array detects full-matches to any one of the polynucleotides in the collection.
 - 25. The collection of claim 23, wherein the array detects mismatches to any one of the polynucleotides in the collection.
- 10 26. The collection of claim 22, wherein the collection is provided in a computer-readable format.
 - 27. A method of treatment comprising administering to a mammalian subject in need thereof a therapeutic amount of a composition comprising a polypeptide of claim 10 or 20 and a pharmaceutically acceptable carrier.
 - 28. A method of treatment comprising administering to a mammalian subject in need thereof a therapeutic amount of a composition comprising an antibody that specifically binds to a polypeptide of claim 10 or 20 and a pharmaceutically acceptable carrier.

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SEQUENCE LISTING

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														ggc		262
cag Gln	gct Ala 50	gtg Val	ccc Pro	gtg Val	ggc ggc	atc Ile 55	cct Pro	gct Ala	gcc Ala	agc Ser	cag Gln 60	cgc Arg	atc Ile	ttc Phe	ctg Leu	310
														gcc Ala		358
cgc Arg	aac Asn	ctc Leu	acc Thr	atc Ile 85	ctg Leu	tgg Trp	ctg Leu	cac His	tcg Ser 90	aat Asn	gtg Val	ctg Leu	gcc Ala	cga Arg 95	att Ile	406
gat Asp	gcg Ala	gct Ala	gcc Ala 100	ttc Phe	act Thr	ggc Gly	ctg Leu	gcc Ala 105	ctc Leu	ctg Leu	gag Glu	cag Gln	ctg Leu 110	gac Asp	ctc Leu	454

PCT/US01/47004 WO 02/44340

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ctg ggc cgc cta cac Leu Gly Arg Leu His 130.				
ctg ggc ccg ggg ctg Leu Gly Pro Gly Leu 145			_	
ctg cag gac aac gcg Leu Gln Asp Asn Ala 165				
ctg ggc aac ctc aca Leu Gly Asn Leu Thr 180			_	_
gtg ccc gag cgc gcc Val Pro Glu Arg Ala 195				
ctg cac cag aac cgc Leu His Gln Asn Arg 210				
ctt ggc cgc ctc atg Leu Gly Arg Leu Met 225				
ctg ccc act gag gcc Leu Pro Thr Glu Ala 245	Leu Ala Pro		_	tga ggc 886
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		gaa Glu					_		_	_			_		_	152
		gtg Val		_				_						_	_	200
_		aag Lys 55				_	_								_	248
		aat Asn														296
		cat His														344
		att Ile														392
		gaa Glu														440
		cac His 135														488
	_	gaa Glu	_	_	_				_	_						536
	_	tct Ser		_		-		_	_					_	_	584
		gaa Glu														632
		caa Gln														680
		ata Ile 215														728
ctt Leu	gta Val 230	gaa Glu	ata Ile	gga Gly	cct Pro	cgt Arg 235	ttt Phe	gtc Val	tta Leu	aat Asn	ctc Leu 240	ata Ile	aag Lys	att Ile	ttc Phe	776

Gln Gly Ser Phe Gly		tat gaa aat cct cac tac cag Tyr Glu Asn Pro His Tyr Gln 255 260	824
		aga tcc atc aca gct gca aaa Arg Ser Ile Thr Ala Ala Lys 270 275	872
		gtg caa aaa ctg aga aag aaa Val Gln Lys Leu Arg Lys Lys 290	920
	_	ccc act gca gat gtt ttt gta Pro Thr Ala Asp Val Phe Val 305	968
		ata cag tgg gta aaa cca gag 1 Ile Gln Trp Val Lys Pro Glu 320	.016
Pro Lys Val Asp Leu		aaa cgg att tac aaa agg caa 1 Lys Arg Ile Tyr Lys Arg Gln 335 340	.064
aga aaa atg aaa cag Arg Lys Met Lys Gln 345		333	.113
gaaacctgat ttgtttttc	a gttactttat at	ttattttg tattcaatgt gtaaatactt 1	173
ttattatcta atactatct	t acgtctaatt ag	tgtagcat ttacaagaaa gaaaaattaa 1	.233
gatcttaaaa tcagtgatt	a totttttota aa	taaaatat caccagaaaa aaaaaa 1	L289

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Ser Thr Met Ser Ala Pro Thr Cys Leu Ala His Leu Pro Pro Cys Phe

5 10 15

ctg ctg ctg gca ctg gtc ctt gtc ccc tca gat gcc tct ggg cag agc
Leu Leu Leu Ala Leu Val Leu Val Pro Ser Asp Ala Ser Gly Gln Ser
20 25 30

age agg aat gac tgg cag gtg cta cag ccc gag ggc ccc atg ctg gtg 201

Ser 35	Arg	Asn	Asp	Trp	Gln 40	Val	Leu	Gln	Pro	Glu 45	Gly	Pro	Met	Leu	Val 50	
gca Ala	gaa Glu	ggt Gly	gag Glu	aca Thr 55	ctt Leu	cta Leu	ctg Leu	agg Arg	tgt Cys 60	atg Met	gtg Val	gt <i>c</i> Val	Gly	tcc Ser 65	tgc Cys	24:
act Thr	gat Asp	ggt Gly	atg Met 70	ata Ile	aaa Lys	tgg Trp	gtg Val	aag Lys 75	atc Ile	gcg Ala	cta Leu	gcg Ala	agc Ser 80	ttt Phe	tat Tyr	29'
gag Glu	gac Asp	gga Gly 85	Gl Y 999	gat Asp	gaa Glu	gac Asp	att Ile 90	gtg Val	acc Thr	att Ile	tcg Ser	cag Gln 95	gca Ala	acc Thr	ccc Pro	34!
agt Ser	tca Ser 100	gtg Val	tcc Ser	aga Arg	ggc	aca Thr 105	gcc Ala	ccc Pro	agt Ser	gat Asp	aat Asn 110	aga Arg	gtg Val	aca Thr	tcc Ser	39 :
ttc Phe 115	aga Arg	gac Asp	ctc Leu	att Ile	cat His 120	gac Asp	caa Gln	gat Asp	gaa Glu	gat Asp 125	gag Glu	gag Glu	gaa Glu	gag Glu	gaa Glu 130	44:
ggc Gly	cag Gln	agg Arg	ttt Phe	tat Tyr 135	gct Ala	GJÀ aaa	ggc Gly	tca Ser	gag Glu 140	aga Arg	agt Ser	gga Gly	cag Gln	cag Gln 145	att Ile	489
gtt Val	ggc Gly	cct Pro	ccc Pro 150	agg Arg	aag Lys	aaa Lys	agt Ser	ccc Pro 155	aac Asn	gag Glu	ctg Leu	gtg Val	gat Asp 160	gat Asp	ctc Leu	. 531
ttt Phe	aaa Lys	ggt Gly 165	gcc Ala	aaa Lys	gag Glu	cat His	gga Gly 170	gct Ala	gta Val	gct Ala	gtg Val	gag Glu 175	cga Arg	gtg Val	acc Thr	585
aag Lys	agc Ser 180	cct Pro	gga Gly	gag Glu	acc Thr	agt Ser 185	aaa Lys	ccg Pro	aga Arg	cca Pro	ttt Phe 190	gca Ala	gga Gly	ggt Gly	ggc	633
tac Tyr 195	cgc Arg	ctt Leu	Gly 999	gca Ala	gca Ala 200	cca Pro	gag Glu	gaa Glu	gag Glu	tct Ser 205	gcc Ala	tat Tyr	gtg Val	gca Ala	gga Gly 210	681
gaa Glu	aag Lys	agg Arg	cag Gln	cat His 215	t.cc Ser	agc Ser	caa Gln	gat Asp	gtt Val 220	cat His	gta Val	gta Val	ttg Leu	aaa Lys 225	ctc Leu	729
tgg Trp	aag Lys	agt Ser	gga Gly 230	ttc Phe	agc Ser	ctg Leu	gat Asp	aat Asn 235	gga Gly	gaa Glu	ctc Leu	aga Arg	agc Ser 240	tac Tyr	caa Gln	777
gac Asp	cca Pro	tcc Ser 245	aat Asn	gcc Ala	cag Gln	ttt Phe	ctg Leu 250	gag Glu	tct Ser	atc Ile	ege Arg	aga Arg 255	GJÀ aaa	gag Glu	gtg Val	825
cca Pro	gca Ala 260	gag Glu	ctt Leu	cgg Arg	agg Arg	cta Leu 265	gct Ala	cac His	ggt Gly	gga Gly	cag Gln 270	gtg Val	aac Asn	ttg Leu	gat Asp	873
atg Met	gag Glu	gac Asp	cat His	cgg Arg	gac Asp	gag Glu	gac Asp	ttt Phe	gtg Val	aag Lys	ccc Pro	aaa Lys	gga Gly	gcc Ala	ctt Leu	921

WO 02/4	4340													P	CT/US	01/47004
275					280					285					290	
caa Gln	gcc Ala	ttc Phe	act Thr	ggc Gly 295	gag Glu	ggt Gly	cag Gln	aaa Lys	ctg Leu 300	ggc ggc	agc Ser	act Thr	gcc Ala	ccc Pro 305	cag Gln	969
				agc Ser												1017 [.]
				atc Ile												1065
				gca Ala												1113
				agc Ser												1161
				acc Thr 375												1209
gag Glu	ctg Leu	gct Ala	gat Asp 390	gag Glu	agc Ser	cag Gln	acc Thr	ctg Leu 395	aag Lys	gaa Glu	gcc Ala	aac Asn	ctg Leu 400	ctc Leu	aat Asn	1257
_	_			cag Gln				taa								1284
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<221> CDS
<222> (38)..(1177)

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Leu Val Leu Val Pro Ser Asp Ala Ser Gly Gln Ser Ser Arg Asn Asp
25 30 35

199

tgg cag gtg cta cag ccc gag ggc ccc atg ctg gtg gca gaa ggt gag

Tr	Gln 40		Leu	Gln	Pro	Glu 45	Gly	Pro	Met	Leu	V al	Ala	Glu	Gly	Glu	
aca Thi	ctt Leu	cta Leu	ctg Leu	agg Arg	tgt Cys 60	atg Met	gtg Val	gtc Val	ggc	tcc Ser 65	tgc Cys	act Thr	gat Asp	ggt Gly	atg Met 70	247
ata Ile	aaa Lys	tgg Trp	gtg Val	aag Lys 75	atc Ile	gcg Ala	cta Leu	gcg Ala	agc Ser 80	ttt Phe	tat Tyr	gag Glu	gac Asp	gga Gly 85	gly ggg	295
gat Asp	gaa Glu	gac Asp	att Ile 90	gtg Val	acc Thr	att Ile	tcg Ser	cag Gln 95	gca Ala	acc Thr	ccc Pro	agt Ser	tca Ser 100	gtg Val	tcc Ser	343
aga Arg	gly Gly	aca Thr 105	gcc Ala	ccc Pro	agt Ser	gat Asp	aat Asn 110	aga Arg	gtg Val	aca Thr	tcc Ser	ttc Phe 115	aga Arg	gac Asp	ctc Leu	391
att Ile	cat His 120	gac Asp	caa Gln	gat Asp	gaa Glu	gat Asp 125	gag Glu	gag Glu	gaa Glu	gag Glu	gaa Glu 130	Gly	cag Gln	agg Arg	ttt Phe	439
tat Tyr 135	gct Ala	gly aaa	ggc	tca Ser	gag Glu 140	aga Arg	agt Ser	gga Gly	cag Gln	cag Gln 145	att Ile	gtt Val	ggc	cct Pro	ccc Pro 150	487
agg	aag Lys	aaa Lys	agt Ser	ccc Pro 155	aac Asn	gag Glu	ctg Leu	gtg Val	gat Asp 160	gat Asp	ctc Leu	ttt Phe	aaa Lys	ggt Gly 165	gcc Ala	535
aaa Lys	gag Glu	cat His	gga Gly 170	gct Ala	gta Val	gct Ala	gtg Val	gag Glu 175	cga Arg	gtg Val	acc Thr	aag Lys	agc Ser 180	cct Pro	gga Gly	583
gag	acc Thr	agt Ser 185	aaa Lys	ccg Pro	aga Arg	gtt Val	cat His 190	gta Val	gta Val	ttg Leu	aaa Lys	ctc Leu 195	tgg Trp	aag Lys	agt Ser	631
gga	ttc Phe 200	agc Ser	ctg Leu	gat Asp	aat Asn	gga Gly 205	gaa Glu	ctc Leu	aga Arg	agc Ser	tac Tyr 210	caa Gln	gac Asp	cca Pro	tcc Ser	679
	gcc Ala															727
ctt Leu	cgg Arg	agg Arg	cta Leu	gct Ala 235	cac His	ggt Gly	gga Gly	cag Gln	gtg Val 240	aac Asn	ttg Leu	gat Asp	atg Met	gag Glu 245	gac Asp	775
cat His	cgg Arg	gac Asp	gag Glu 250	gac Asp	ttt Phe	gtg Val	r As T	ccc Pro 255	aaa Lys	gga Gly	gcc Ala	ttc Phe	aaa Lys 260	gcc Ala	ttc Phe	823
act	ggc	gag Glu 265	ggt Gly	cag Gln	aaa Lys	ctg Leu	ggc Gly 270	agc Ser	act Thr	gcc Ala	ccc Pro	cag Gln 275	gtg Val	ttg Leu	agt Ser	871
acc Thr	agc Ser	tct Ser	cca Pro	gcc Ala	caa Gln	cag Gln	gca Ala	gaa Glu	aat Asn	gaa Glu	gcc Ala	aaa Lys	gcc Ala	agc Ser	tct Ser	919

WO 02/44340

280

285

290

tcc atc tta atc gac gaa tca gag cct acc aca aac atc caa att cgg
Ser Ile Leu Ile Asp Glu Ser Glu Pro Thr Thr Asp Ile Glp Ile Arg

							- V-									
tcc Ser 295	atc Ile	tta Leu	atc Ile	gac Asp	gaa Glu 300	tca Ser	gag Glu	cct Pro	acc Thr	aca Thr 305	aac Asn	atc Ile	caa Gln	att Ile	cgg Arg 310	967
ctt Leu	gca Ala	gac Asp	ggc Gly	999 Gly 315	agg Arg	ctg Leu	gtg Val	cag Gln	aaa Lys 320	ttt Phe	aac Asn	cac His	agc Ser	cac His 325	agg Arg	1015
atc Ile	agc Ser	gac Asp	atc Ile 330	cga Arg	ctc Leu	ttc Phe	atc Ile	gtg Val 335	gat Asp	gcc Ala	cgg Arg	cca Pro	gcc Ala 340	atg Met	gct Ala	1063
gcc Ala	acc Thr	agc Ser 345	ttt Phe	atc Ile	ct <i>c</i> Leu	atg Met	act Thr 350	act Thr	ttc Phe	ccg Pro	aac Asn	aaa Lys 355	gag Glu	ctg Leu	gct Ala	1111
		agc Ser														1159
		cgg Arg			taa	ccg	ecc a	agcca	gctg	gc ct	ggc	etec	e te	etgtg	gttt	1213
ccca	tggc	cca g	gtggd	cate	ge ed	cate	9999	a teg	jecec	etcc	tgc	ccct	tg t	gcad	caccca	1273
gcag	tcca	agt s	gcaac	egtet	c ct	ccat	agct	cto	ggtt	ctt	agat	ctte	ggt t	ggad	gtttg	1333
tttt	ctcc	ett a	gtto	gcatt	t co	tggg	gttt	: t								1364

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tggaaggcgc acggggcgaa g atg gcg gcg gag cga cag gag gcg ctg agg 171
Met Ala Ala Glu Arg Gln Glu Ala Leu Arg

gag ttc gtg gcg gtg acg gcc gag gag gac cgg gcc cgc ttc ttt 219 Glu Phe Val Ala Val Thr Gly Ala Glu Glu Asp Arg Ala Arg Phe Phe 15 20 25

ctc gag tcg gcc ggc tgg gac ttg cag atc gcg cta gcg agc ttt tat 267 Leu Glu Ser Ala Gly Trp Asp Leu Gln Ile Ala Leu Ala Ser Phe Tyr 30 ... 35 40

gag gac gga ggg gat gaa gac att gtg aco att tcg cag gca acc ccc Glu Asp Gly Gly Asp Glu Asp Ile Val Thr Ile Ser Gln Ala Thr Pro 45 50 55	315
agt tca gtg tcc aga ggc aca gcc ccc agt gat aat aga gtg aca tcc Ser Ser Val Ser Arg Gly Thr Ala Pro Ser Asp Asn Arg Val Thr Ser 60 65 70	363
ttc aga gac ctc att cat gac caa gat gaa gat gag gaa gag gaa Phe Arg Asp Leu Ile His Asp Gln Asp Glu Asp Glu Glu Glu Glu 75 80 85 90	411
ggc cag agg agc agg ttt tat gct ggg ggc tca gag aga agt gga cag Gly Gln Arg Ser Arg Phe Tyr Ala Gly Gly Ser Glu Arg Ser Gly Gln 95 100 105	459
cag att gtt ggc cct ccc agg aag aaa agt ccc aac gag ctg gtg gat Gln Ile Val Gly Pro Pro Arg Lys Lys Ser Pro Asn Glu Leu Val Asp 110 115 120	507
gat ctc ttt aaa ggt gcc aaa gag cat gga gct gta gct gtg gag cga Asp Leu Phe Lys Gly Ala Lys Glu His Gly Ala Val Ala Val Glu Arg 125 130 135	555
gtg acc aag agc cct gga gag acc agt aaa ccg aga cca ttt gca gga Val Thr Lys Ser Pro Gly Glu Thr Ser Lys Pro Arg Pro Phe Ala Gly 140 145 150	603
ggt ggc tac cgc ctt ggg gcc agc acc aga gga aga gtc tgc cta tgt Gly Gly Tyr Arg Leu Gly Ala Ser Thr Arg Gly Arg Val Cys Leu Cys 155 160 165 170	651
ggc agg aga aaa gag gca gca ttc cag cca aga tgt tca tgt agt att Gly Arg Arg Lys Glu Ala Ala Phe Gln Pro Arg Cys Ser Cys Ser Ile 175 180 185	699
gaa act ctg gaa gag tgg att cag cct gga taa tggagaac tcagaagcta Glu Thr Leu Glu Glu Trp Ile Gln Pro Gly 190 195	750
ccaagaccca tccaatgccc agtttctgga gtctattcgc agaggggagg tgcagcagag	810
cttccgaggc tagcctcacg tggacaggtg aacttggata tggaggacca tcgggacgag	870
gactttgtga agcccaaagg agccttcaaa gccttcactg gcgagggtca gaaactgggc	930
agcactgccc cccaggtgtt gagtaccagc tctccagccc aacaggcaga aaatgaagcc	990
aaagccagct cttccatctt aatcgacgaa tcagagccta ccacaaacat ccaaattcgg	1050
cttgcagacg gcgggaggct ggtgcagaaa tttaaccaca gccacaggat cagcgacatc	1110
cgactcttca tcgtggatgc ccggccagcc atggctgcca ccagctttat cctcatgact	1170
actttcccga acaaagagct ggctgatgag agccagaccc tgaaggaagc caacctgctc	1230
aatgctgtca tegtgcageg gttaacataa	1260

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                                                                       58
ttc gcc ccc cgg ctg ctg gat ttg cag aag acg aaa tac gcg agg ttc
                                                                      106
Phe Ala Pro Arg Leu Leu Asp Leu Gln Lys Thr Lys Tyr Ala Arg Phe
atg aac cac cga gtc cct gcc cac aag agg tac cag ccc aca gag tat
                                                                      154
Met Asn His Arg Val Pro Ala His Lys Arg Tyr Gln Pro Thr Glu Tyr
                             25
gaa cat geg gee aac tgt gee ace cat get tte tgg ate ate eee age
                                                                      202
Glu His Ala Ala Asn Cys Ala Thr His Ala Phe Trp Ile Ile Pro Ser
                         40
atc ctg ggc agc tcc aac ctc tac ttc ctg tcg gac gat gac tgg gag
                                                                      250
Ile Leu Gly Ser Ser Asn Leu Tyr Phe Leu Ser Asp Asp Trp Glu
acc atc tct gcc tgg atc tac ggc ctc ggc ctc tgc ggc ctc ttc gtg
                                                                      298
Thr Ile Ser Ala Trp Ile Tyr Gly Leu Gly Leu Cys Gly Leu Phe Val
gtg tcc act gtg ttt cac acc atc tcc tgg aag aag agc cac ctc aga
                                                                      346
Val Ser Thr Val Phe His Thr Ile Ser Trp Lys Lys Ser His Leu Arg
                                 90
tgg gga ttc tga ggg ccaaggggtc ttggctggac agaggagccc agccctgcta
                                                                      401
Trp Gly Phe
acctgtaggc aggcacgatc agtccagggc acggctctgn gggcactggc ccttccttgc
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ttgcaggggc tg
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<220> <221> CDS

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ttcaagagca	agacaggag	g cgactg	Me	_	tgg ctg Trp Leu 5	Arg His		171
gtc ctc cac Val Leu Glr 10				_				219
aag cca gca Lys Pro Ala 25								267
gcc atc ago Ala Ile Sei							_	315
cat gat gto								363
ccc cca aat Pro Pro Asi 75	n Pro Ala							411
aag tgg ago Lys Trp Ser 90				_		_		459
gtg ctg ggg Val Leu Gly 105					_		_	507
gta ctc cca Val Leu Pro						-	_	555
cgg aca ggg Arg Thr Gl								603
gac ctc aag Asp Leu Lys 15	s Tyr Arg							651
agt gac too Ser Asp Ser 170								699
tcc ctc cas Ser Leu Gli 185	-							747
ttg aac tte Leu Asn Phe								795

	•			205					210					215		
atg Met	agg Arg	aca Thr	aag Lys 220	agt Ser	cga Arg	gac Asp	ccg Pro	ctg Leu 225	gcc Ala	atc Ile	tac Tyr	ttt Phe	acc Thr 230	aag Lys	cgg Arg	843
gaa Glu	cca Pro	ccg Pro 235	ej aaa	gcc Ala	ccc Pro	aag Lys	atg Met 240	gtc Val	gag Glu	cac His	tcc Ser	cag Gln 245	agc Ser	agc Ser	tac Tyr	891
gga Gly	ctg Leu 250	ggt Gly	ttt Phe	gtg Val	gcc Ala	agc Ser 255	gga Gly	aga Arg	cgg Arg	tgg Trp	gtg Val 260	gcc Ala	ttg Leu	acc Thr	gaa Glu	939
tct Ser 265	gac Asp	atc Ile	ttc Phe	tgg Trp	aac Asn 270	acg Thr	act Thr	gac Asp	act Thr	ggc Gly 275	tgg Trp	gtg Val	aag Lys	gca Ala	gcc Ala 280	987
tgg Trp	act Thr	ctc Leu	ttc Phe	tct Ser 285	gcc Ala	tgg Trp	cct Pro	aat Asn	gga Gly 290	tct Ser	tgc Cys	att Ile	ttt Phe	gtg Val 295	cat His	1035
gag Glu	ctg Leu	ccc Pro	cga Arg 300	gtt Val	gat Asp	gcc Ala	aaa Lys	gtt Val 305	atc Ile	ctg Leu	aat Asn	act Thr	ctc Leu 310	tcc Ser	aaa Lys	1083
ttc Phe	ccg Pro	ata Ile 315	acc Thr	acc Thr	ctc Leu	tgc Cys	tgt Cys 320	gtc Val	cca Pro	acc Thr	atc Ile	ttt Phe 325	cgg Arg	ctg Leu	ctt Leu	1131
gtg Val	cag Gln 330	gag Glu	gat Asp	ctg Leu	acc Thr	agg Arg 335	tac Tyr	cag Gln	ttt Phe	cag Gln	agc Ser 340	ttg Leu	agg Arg	cac His	tgt Cys	1179
ctg Leu 345	acc Thr	gga Gly	gga Gly	gag Glu	gcc Ala 350	ctc Leu	aac Asn	cct Pro	gac Asp	gtg Val 355	agg Arg	gag Glu	aag Lys	tgg Trp	aaa Lys 360	1227
cac His	cag Gln	act Thr	ggt Gly	gtg Val 365	gag Glu	ctg Leu	tac Tyr	gaa Glu	ggc Gly 370	tat Tyr	Gly ggc	cag Gln	tct Ser	gaa Glu 375	acg Thr	1275
gtt Val	gtc Val	atc Ile	tgt Cys 380	gcc Ala	aat Asn	cca Pro	aaa Lys	ggc Gly 385	atg Met	aaa Lys	atc Ile	aag Lys	tct Ser 390	gga Gly	tcc Ser	1323
atg Met	Gly 999	aag Lys 395	gcg Ala	tcc Ser	cca Pro	ccc Pro	tac Tyr 400	gat Asp	gtg Val	cag Gln	att Ile	gtg Val 405	gat Asp	gat Asp	gag Glu	1371
Gly	aac Asn 410	gtc Val	ctg Leu	cct Pro	cct Pro	gga Gly 415	gaa Glu	gag Glu	gjå aaa	aat Asn	gtt Val 420	gcc Ala	gtc Val	cgt Arg	atc Ile	1419
aga Arg 425	ccc Pro	act Thr	cgg Arg	ccc Pro	ttc Phe 430	tgt Cys	ttc Phe	ttc Phe	aat Asn	tgc Cys 435	tat Tyr	ttg Leu	gac Asp	aat Asn	cct Pro 440	1467
gag Glu	aag Lys	aca Thr	gct Ala	gca Ala 445	tca Ser	gaa Glu	caa Gln	Gly 999	gac Asp 450	ttt Phe	tac Tyr	atc Ile	aca Thr	999 Gly 455	gac Asp	1515

cga gct cgc atg gac aag gat ggc tac ttt tgg ttc atg gga aga aac Arg Ala Arg Met Asp Lys Asp Gly Tyr Phe Trp Phe Met Gly Arg Asn 460 465 470	1563
gac gat gtg atc aat tct tca agc tac cgg atc ggg cct gtt gaa gtg Asp Asp Val Ile Asn Ser Ser Ser Tyr Arg Ile Gly Pro Val Glu Val 475 480 485	1611
gaa agt gcc ctg gca gag cat cct gct gtc ctg gag tcg gct gtg gtc Glu Ser Ala Leu Ala Glu His Pro Ala Val Leu Glu Ser Ala Val Val 490 495 500	1659
agc agc cca gac ccc atc agg gga gag gtg gta aag gca ttt ata gtc Ser Ser Pro Asp Pro Ile Arg Gly Glu Val Val Lys Ala Phe Ile Val 505 510 515	1707
ctt act cca gcc tac tcc tct cat gac cca gag gca cta acg cgg gaa Leu Thr Pro Ala Tyr Ser Ser His Asp Pro Glu Ala Leu Thr Arg Glu 525 530 535	1755
ctc cag gag cat gtg aaa agg gtg act gct cca tac aaa tac ccc agg Leu Gln Glu His Val Lys Arg Val Thr Ala Pro Tyr Lys Tyr Pro Arg 540 545 550	1803
aag gtg gcc ttt gtt tca gaa ctg cca aag acg gtt tct gga aag atc Lys Val Ala Phe Val Ser Glu Leu Pro Lys Thr Val Ser Gly Lys Ile 555 560 565	1851
caa agg agt aaa ttg cga agt cag gag tgg ggg aaa tga ggtgcacccc Gln Arg Ser Lys Leu Arg Ser Gln Glu Trp Gly Lys 570 575 580	1900
aggaaggeee egtagaeete egaagaetee acaagaaaet aatggateae tggteagtee	1960
ccatggggag catcatetet tegaceetaa agatgteaaa ggtgtgeage ttecaaaegg	2020
catececagg ateaetggge aatgetggaa agageaaaag aatateattg geeetgatea	2080
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cttcatcctt tgtatgtaac catttggcaa aagtatgcag gaacataaaa taaaatatcc	2320
tttagctcag aaattctatc ttcgggagtc accacaaaag aaaaaaatca aaatgcagaa	2380
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ttc acg gac acc ttc aac atg gac acc agg aag Phe Thr Asp Thr Phe Asn Met Asp Thr Arg Lys 20 25			151
ggc tcc agg acc gcc ttc ttt ggc tac aca gtg Gly Ser Arg Thr Ala Phe Phe Gly Tyr Thr Val 35 40 45			199
agt ggc aat aag tgg ctg gtc gtg ggc gcc cca Ser Gly Asn Lys Trp Leu Val Val Gly Ala Pro 55 60			247
tac cag aag acg gga gac gtg tac aag tgt cca Tyr Gln Lys Thr Gly Asp Val Tyr Lys Cys Pro 70 75			295
tgc acc aaa ctc aac ctg ggt aac gtg ggc tgg Cys Thr Lys Leu Asn Leu Gly Asn Val Gly Trp 85 90	tgg tct ctt Trp Ser Leu 95	cac aat His Asn	343
gag gcc agc ggt tgt cta aca caa ggc agg ctc Glu Ala Ser Gly Cys Leu Thr Gln Gly Arg Leu 100 105		cccatgtc	393
catggtcaca ctgactcctt cctgctactc catgagatga	cccagctgat	atcactgccc	453
ccactttaca catgaggaag ctgaggccag ggagaggagg	caacttttcc	acagtcacac	513
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ct <i>c</i> Leu	ttc Phe	ctg Leu	ggc Gly 115	acg Thr	ttc Phe	ttc Phe	att Ile	agc Ser 120	tcc Ser	ggc Gly	ctc Leu	atc Ile	ctc Leu 125	tcc Ser	gta Val	622
gct Ala	ej aaa	ttc Phe 130	ttc Phe	tac Tyr	ctc Leu	aag Lys	cgc Arg 135	tcc Ser	agt Ser	aaa Lys	ctc Leu	ccc Pro 140	agg Arg	gcc Ala	tgc Cys	670
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	_		_	_		_	_				_		cgg Arg			144	:
	_				_	_		_		_			atg Met	_		192	!
_					_		_	_	_				gaa Glu			240	ţ
		_				_				_			tcg Ser			288	ţ
													ctg Leu 110			336	į
	_		_				_				_	_	acg Thr	_	_	384	ŧ
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	_	_	_		_	_			_				GJ À aaa			480)
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cgc Arg	tgt Cys	gtc Val	tgc Cys	aac Asn 885	ctg Leu	ggt Gly	tat Tyr	gag Glu	gca Ala 890	ggt Gl <u>y</u>	gcc Ala	tca Ser	Gly	aag Lys 895	gac Asp		2688
tgc Cys	aca Thr	gac Asp	gtg Val 900	gat Asp	gag Glu	tgt Cys	gcc Ala	ctc Leu 905	aac Asn	agc Ser	ctc Leu	ctg Leu	tgt Cys 910	gac Asp	aac Asn		2736
G] A aaa	tgg Trp	tgc Cys 915	cag Gln	aat Asn	agc Ser	cct Pro	ggc Gly 920	agc Ser	tac Tyr	agc Ser	tgc Cys	tcc Ser 925	tgc Cys	ccc Pro	ccc Pro		2784
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tgc Cys 945	ctg Leu	tcc Ser	agc Ser	ccg Pro	tgt Cys 950	gtg Val	agt Ser	ggc ggc	gtc Val	tgt Cys 955	cgg Arg	aac Asn	ctg Leu	gcc Ala	ggc Gly 960		2880
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Cys	tgc Cys 1010	gcc			Gly	gca	gcc			Ser	ccc	tgc				3072
	atc Ile		_	Ile				_	Ser	_	_		_	Gly		3120
	ctc Leu		Gly					Leu					Lys			3168
	ctc Leu	Phe			_		Pro	_	_	_	_	Thr			_	3216
	gtc Val					Val					Ser					3264
Ser	Gly ggc				Asn					Tyr						3312
	ggc Gly	_		Leu	_				Thr		-		_	Ser		3360
	ggc Gly		Cys					Gln					Glu			3408
ctt								•								
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Leu	Gln tgg Trp	gly	Ala 1140 agc	Ser	Leu	Arg gaa Glu	Ser	gag Glu 1145 tgc	tgc Cys gag	Cys	Ala gac Asp	Thr : cct	ctc Leu 150 gcc	Gly	Ala	3456 3504
gcc Ala cgg Arg	Gln tgg Trp	ggg Gly 1155	Ala 1140 agc Ser	Ser ccc Pro	tgc Cys atg	Arg gaa Glu acg	Ser cgc Arg 1160	gag Glu 1145 tgc Cys	tgc Cys gag Glu	Cys atc Ile tgc Cys	Ala gac Asp	Thr cct Pro 1165	ctc Leu 150 gcc Ala	Gly tgt Cys	Ala gcc Ala gag	
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Trp Asp Glu Asp Glu Cys Gly Val Thr Leu Pro Gly Lys Tyr Arg Met 1235 1240 1245	
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gcc tgc ccg gat ccc gag tct ctg gag ttc gcc agc ctg tgc ccg cgg Ala Cys Pro Asp Pro Glu Ser Leu Glu Phe Ala Ser Leu Cys Pro Arg 1265 1270 1275 1280	3840
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cag tgt ccc cct ggg cat gag ctg acg gcc aag ggc act gcc tgt gag Gln Cys Pro Pro Gly His Glu Leu Thr Ala Lys Gly Thr Ala Cys Glu 1410 1415 1420	4272
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1475 1480 1485

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5 10 15 20

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gcc Ala	gtg Val 70	ctg Leu	ctg Leu	ccc Pro	atc Ile	ctg Leu 75	ggt Gly	acc Thr	tcg Ser	tgg Trp	gtc Val 80	ttt Phe	ggc Gly	gtg Val	ctt Leu	294
gct Ala 85	gtc Val	aac Asn	ggt Gly	tgt Cys	gct Ala 90	gtg Val	gtt Val	ttc Phe	cag Gln	tac Tyr 95	atg Met	ttt Phe	gcc Ala	acg Thr	ctc Leu 100	342
aac Asn	tcc Ser	ctg Leu	cag Gln	gga Gly 105	ctg Leu	ttc Phe	ata Ile	ttc Phe	ctc Leu 110	ttt Phe	cat His	tgt Cys	ctc Leu	ctg Leu 115	aat Asn	390
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acg Thr	agc Ser	agc Ser 135	tcc Ser	gcc Ala	cgc Arg	acc Thr	tcc Ser 140	aac Asn	gcg Ala	aag Lys	ccc Pro	ttc Phe 145	cac His	tcg Ser	gac Asp	486
ctc Leu	atg Met 150	aat Asn	Gl A aaa	acc Thr	cgg Arg	cca Pro 155	ggc Gly	atg Met	gcc Ala	tcc Ser	acc Thr 160	aag Lys	ctc Leu	agc Ser	cct Pro	534
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nnnn	ınnnn	inn a	naca	nnng	n no	tnnn	ctgn	nga	ctct	gct	gtcg	gago	ac a	ctgo	tcatc	759
ccag	caac	ct g	atgo	ccag	g co	agcg	tggg	ccc	tcct	gcc	ttga	atac	ac c	cgtg	ggctg	819
agtg	actt	.cc t	cggg	ggat	t co	cagg	acac	agt	ggcc	tga	ctgt	gatg	gt g	ccct	tgagc	879
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															tgtga	1059
ggta	aaac	ta t	cgga	gaco	c ca	ctgt	ttga	atc	catc	gat	gtgg	aaag	tt c	cccc	aagcc	1119
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	_		Gly	_	_	_	_		_	-			_			103
			cgc Arg 25													151
-			tgt Cys			_					_			_	_	199
			gag Glu													247
			atc Ile													295
			ctc Leu													343
			gag Glu 105													391
		Thr	gat Asp	Gly	Ser	Ile	Ser	Gln	Phe	Arg	Asn	Trp	Tyr			439
	-		tgc Cys		_		_	_		_	_			_		487
_	_		gct Ala									_			_	535
			aac Asn		Lys											583

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atc Ile 230	ccc Pro	agc Ser	att Ile	ccc Pro	ctt Leu 235	ctc Leu	ctc Leu	ctc Leu	ctt Leu	gtg Val 240	gtc Val	acc Thr	aca Thr	gtt Val	gta Val 245	775
	tgg Trp															823
	aca Thr															871
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	gct Ala															1063
gag Glu	agt Ser	gga Gly	ttt Phe 345	gtg Val	acc Thr	aat Asn	gac Asp	att Ile 350	tat Tyr	gag Glu	ttc Phe	tcc Ser	cca Pro 355	gac Asp	caa Gln	1111
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tat Tyr	tag	gaca	atata	aaa a	aact	gaaa	ac t <u>e</u>	gacaa	caat	gga	aaag	jaaa	tgat	aago	caa	1215
aat	cctct	ta t	ttt	ctata	aa gg	gaaaa	ataca	a cag	gaagg	gtat	atga	acaa	agc t	taga	atcagg	1275
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gca	cata	qta d	aato	ctcaa	at aa	atat	cact	: tac	rttac	rtta	tato	taac	abb t	taac	rogaca	1455

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	gcc Ala	cgc Arg	tgt Cys	gaa Glu 180	gtc Val	cag Gln	ttc Phe	tct Ser	cca Pro 185	cgt Arg	tgt Cys	cct Pro	gaa Glu	gat Asp 190	tct Ser	gtt Val	576
	ctg Leu	atc Ile	gag Glu 195	ggt Gly	tat Tyr	gct Ala	cct Pro	cct Pro 200	Gly 999	gag Glu	tgc Cys	tgt Cys	ccc Pro 205	tta Leu	ccc Pro	agc Ser	624
	cgc Arg	tgc Cys 210	gtg Val	tgc Cys	aac Asn	ccc Pro	gca Ala 215	ggc	tgt Cys	ctg Leu	cgc Arg	aaa Lys 220	gtc Val	tgc Cys	cag Gln	ccg Pro	672
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	gag Glu 305	gtg Val	gga Gly	tcc Ser	act Thr	ccc Pro 310	cgc Arg	ata Ile	gtc Val	tct Ser	cgt Arg 315	gly ggc	gat Asp	gjå aaa	aca Thr	cct Pro 320	960
	gga Gly	aag Lys	tgc Cys	tgt Cys	gat Asp 325	gtc Val	ttt Phe	gaa Glu	tgt Cys	gtt Val 330	aat Asn	gat Asp	aca Thr	aag Lys	cca Pro 335	gcc Ala	1008
	tgc Cys	gta Val	ttt Phe	aac Asn 340	aat Asn	gtg Val	gaa Glu	tat Tyr	tat Tyr 345	gat Asp	gga Gly	gac Asp	atg Met	ttt Phe 350	cga Arg	atg Met	1056
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cac tgc gtt gcg acc gtc tgc gga cag acc tgc aca aac cct gtg aaa His Cys Val Ala Thr Val Cys Gly Gln Thr Cys Thr Asn Pro Val Lys 435 440 445	1344
gtg cct ggg gag tgt tgc cct gtg tgc gaa gaa cca acc atc atc aca Val Pro Gly Glu Cys Cys Pro Val Cys Glu Glu Pro Thr Ile Ile Thr 450 455 460	1392
gtt gat cca cct gca tgt ggg gag tta tca aac tgc act ctg aca ggg Val Asp Pro Pro Ala Cys Gly Glu Leu Ser Asn Cys Thr Leu Thr Gly 465 470 475 480	1440
aag gac tgc att aat ggt ttc aaa cgc gat cac aat ggt tgt cgg acc Lys Asp Cys Ile Asn Gly Phe Lys Arg Asp His Asn Gly Cys Arg Thr 485 490 495	1488
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aat Asn	cag Gln	aaa Lys	gac Asp	cgc Arg 85	Thr	ttc Phe	act Thr	gtg Val	acc Thr 90	Met	gag Glu	gl y aaa	ctc Leu	agg Arg 95	cga Arg	408
gat Asp	gac Asp	gca Ala	gat Asp 100	Val	tac Tyr	tgg Trp	tgt Cys	102 GJA 333	att Ile	gaa Glu	aga Arg	aga Arg	gga Gly 110	cct Pro	gac Asp	456
ctt Leu	gjà aaa	act Thr 115	caa Gln	gtg Val	aaa Lys	gtg Val	att Ile 120	gtt Val	gac Asp	cca Pro	tag	gga	g eg	gctt	cctc	506
aaca	gcaa	agc 1	tcac	ctac	ca a	cagca	aata	t gg	cagt	gttg	atc	ggct	ccc :	acaa	gaggaa	566
															tgccat	626
				ggta			gtcc	c tga	agga	gcca	999	gaac	agc (ctate	ctacat	686
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ggcc													Met 1	Ser	tgt Cys	116
atc Ile	ttg Leu 5	gga Gly	ttc Phe	tgt Cys	ttt Phe	cca Pro 10	ggc Gly	tgt Cys	ttc Phe	tcc Ser	atc Ile 15	caa Gln	ggc Gly	cca Pro	gag Glu	164
ser 20	gtg Val	aga Arg	gcc Ala	cca Pro	gag Glu 25	cag Gln	gj aaa	tcc Ser	ctg Leu	acg Thr 30	gtt Val	caa Gln	tgc Cys	cac His	tat Tyr 35	212
aag Lys (caa Gln	gga Gly	tgg Trp	gag Glu 40	acc Thr	tac Tyr	att Ile	aag Lys	tgg Trp 45	tgg Trp	tgc Cys	cga Arg	gjå aaa	gtg Val 50	cgc Arg	260
tgg (Trp)	gat Asp	aca Thr	tgc Cys	aag Lys	atc Ile	ctc Leu	att Ile	gaa Glu	acc Thr	aga Arg	gly aaa	tcg Ser	gag Glu	caa Gln	gga Gly	308

60

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														gtt Val		404
														gtg Val		452
			gac Asp		tag	ggag	lca č	gette	ctca	ia ca	ıgcaa	geto	aco	ctaco	caac	506
agca	atat	gg d	agto	gttga	at cg	gcto	ccac	aag	gagga	acc	acta	cate	gat d	cctgg	gtattt	566
gtga	aggt	gc d	cato	ttgo	et ca	tctt	ggto	act	gcca	tcc	tcts	gttg	gaa g	ggggt	ctcag	626
aggg	gteec	etg a	aggag	gccag	gg gg	raaca	geet	ato	ctaca	itga	actt	ctcc	ga a	accto	ctgact	686
aa																688

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30

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25

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						gl ^a aaa										429
						gtg Val										477
tca Ser	gat Asp	ctc Leu 85	ctg Leu	ttc Phe	ata Ile	agc Ser	acg Thr 90	ctt Leu	ccc Pro	ttc Phe	agg Arg	gct Ala 95	gac Asp	tat Tyr	tat Tyr	525
ctt Leu	aga Arg 100	ggc	tcc Ser	aat Asn	tgg Trp	ata Ile 105	ttt Phe	gga Gly	gac Asp	ctg Leu	gcc Ala 110	tgc Cys	agg Arg	att Ile	atg Met	573
tct Ser 115	tat Tyr	tcc Ser	ttg Leu	tat Tyr	gtc Val 120	aac Asn	atg Met	tac Tyr	agc Ser	agt Ser 125	att Ile	tat Tyr	ttc Phe	ctg Leu	acc Thr 130	621
						ttc Phe										669
ctg Leu	cat His	gtc Val	acc Thr 150	agc Ser	atc Ile	agg Arg	agt Ser	gcc Ala 155	tgg Trp	atc Ile	ctc Leu	tgt Cys	999 Gly 160	atc Ile	ata Ile	717
						tcc Ser										765
			_	_	_	aca Thr 185		_			_					813
att Ile 195	gct Ala	aag Lys	ctg Leu	cag Gln	acc Thr 200	atg Met	aac Asn	tat Tyr	att Ile	gcc Ala 205	ttg Leu	gtg Val	gtg Val	Gly	tgc Cys 210	861
						ctc Leu										909
gtt Val	ctg Leu	tta Leu	aaa Lys 230	gtg V al	gag Glu	gtc Val	cca Pro	gaa Glu 235	tcg Ser	Gly ggg	ctg Leu	cgg Arg	gtt Val 240	tct Ser	cac His	957
						atc Ile										1005
						aca Thr 265										1053
aaa	gtg	ggt	tta	tgc	aaa	gac	aga	ctg	cat	aaa	gct	ttg	gtt	atc	aca	1101

Lys Val 275	Gly	Leu	Cys	Lys 280	qaA	Arg	Leu	His	Lys 285	Ala	Leu	Val	Ile	Thr 290	
ctg gcc Leu Ala															1149
ttt gct Phe Ala															1197
ggc cat Gly His															1245
tgg ttg Trp Leu 340							taa	gga	ge to	cttag	gatga	a ga	cctgl	ttct	1297
tgtatcct	tg t	tgtc	catc	tt c	attca	actca	a taa	agtt	ctcc	aaat	gac	ctt 9	gtati	ttacat	1357
cactccc	aac a	aaat	gttga	at to	cttaa	atati	t tag	gttg	acca	tta	cttt	tgt i	taata	aagacc	1417
tacttcaa	aaa a	attt	tnnnı	nn ni	nnnı	nnnn	nnı	nnnn	nggg	9999	ggcc	gtt 1	ttaaa	aggacc	1477
cctgggg	ggc (ccaa	attt	ta c	ccgg	gctg	g ca	agga	aaaa	gtt	tttt	ect 1	tata	gggggc	1537
cgtttta	aaa d	ccta	cctg	gg a	attti	ttgg	a aag	gaac	cctt	att	ttgg		ggga	acatat	1597
tgggccaa	acc 1	tecei	tcca	aa a	tttaa	aagg	e tti	tagg	gnnn	nnnı	nnnn	ntt i	ttaaa	agggaa	1657
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tcg Ser	gtg Val	gat Asp	ctg Leu 20	cag Gln	gga Gly	gac Asp	agc Ser	tcc Ser 25	tta Leu	cag Gln	gtg Val	gag Glu	att Ile 30	Ser	gac Asp	512
gca Ala	gtg Val	agt Ser 35	gag Glu	cgg Arg	gac Asp	aag Lys	gtg Val 40	Lys	ttc Phe	act Thr	gtt Val	caa Gln 45	aca Thr	aag Lys	agc Ser	560
tgc Cys	ctc Leu 50	cct Pro	cac His	ttc Phe	gcc Ala	cag Gln 55	acc Thr	gag Glu	ttc Phe	tca Ser	gtc Val 60	gtg Val	cgg Arg	cag Gln	cac His	608
gag Glu 65	gag Glu	ttc Phe	atc Ile	tgg Trp	ctg Leu 70	cat His	gat Asp	gcc Ala	tac Tyr	gtg Val 75	gag Glu	aat Asn	gag Glu	gag Glu	tac Tyr 80	656
gcc Ala	Gly	ctc Leu	atc Ile	atc Ile 85	ccc Pro	cca Pro	gcc Ala	cct Pro	ccg Pro 90	agg Arg	cca Pro	gac Asp	ttt Phe	gag Glu 95	gct Ala	704
tcg Ser	agg Arg	gaa Glu	aag Lys 100	cta Leu	cag Gln	aaa Lys	ttg Leu	ggc Gly 105	gag Glu	GJ Å aaa	gac Asp	agc Ser	tct Ser 110	gtc Val	act Thr	752
cgg Arg	gaa Glu	gag Glu 115	ttt Phe	gcc Ala	aag Lys	atg Met	aag Lys 120	cag Gln	gag Glu	ctg Leu	gaa Glu	gcg Ala 125	gag Glu	tac Tyr	ctg Leu	800
gcc Ala	atc Ile 130	ttt Phe	aag Lys	aag Lys	aca Thr	gtt Val 135	gcg Ala	atg Met	cac His	gaa Glu	gtc Val 140	ttt Phe	ctg Leu	cag Gln	cgc Arg	848
ctg Leu 145	gcg Ala	gcc Ala	cac His	ccc Pro	acc Thr 150	ctg Leu	cgt Arg	cga Arg	gac Asp	cac His 155	aac Asn	ttc Phe	ttt Phe	gtg Val	ttt Phe 160	896
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ctc Leu	ctc Leu	gga Gly	999 Gly 180	ttt Phe	ctg Leu	agg Arg	aat Asn	att Ile 185	gtg V al	aag Lys	tcc Ser	gcg Ala	gat Asp 190	gaa Glu	gcc Ala	992
ctc Leu	atc Ile	acg Thr 195	ggc Gly	atg Met	tca Ser	gly aaa	ctc Leu 200	aag Lys	gag Glu	gtg Val	gat Asp	gac Asp 205	ttc Phe	ttt Phe	gag Glu	1040
cat His	gag Glu 210	agg Arg	acc Thr	ttc Phe	ctg Leu	ttg Leu 215	gag Glu	tat Tyr	cac His	acc Thr	cgt Arg 220	atc Ile	cga Arg	gat Asp	gcc Ala	1088
tgc Cys 225	ctg Leu	Arg	gcc Ala	gac Asp	cgc Arg 230	gtc Val	atg Met	cgc Arg	gcc Ala	cac His 235	aag Lys	tgc Cys	ctg Leu	gca Ala	gac Asp 240	1136
gat Asp	tat Tyr	atc Ile	cct Pro	atc Ile 245	tca Ser	gct Ala	gcg Ala	ctg Leu	agc Ser 250	agt Ser	ctg Leu	gga Gly	aca Thr	cag Gln 255	gaa Glu	1184

					acg Thr											1	.232
					gag Glu											3	280
					agg Arg											1	1328
-	_	-			cgg Arg 310			_	_	-	_				_	1	.376
	_		_	_	aag Lys		_									1	L424
					cag Gln											1	1472
					gag Glu											1	1520
		_	_		ctc Leu			_	_		_					:	1568
					ctg Leu 390											3	1616
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<213> Homo sapiens

<220>

<221> CDS

<222> (1)..(2421)

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gcc gct gcc tcc caa gcc gag gtc gag tcc gag gca gga tgg ggc atg 96
Ala Ala Ser Gln Ala Glu Val Glu Ser Glu Ala Gly Trp Gly Met

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gtg Val	acg Thr	cct Pro 35	gat Asp	ctg Leu	ctc Leu	ttc Phe	gcc Ala 40		gj A aaa	acc Thr	gca Ala	gcc Ala 45	tac Tyr	gcg Ala	cgc Arg	144
gly aaa	gac Asp 50	tgg Trp	ccc Pro	GJA aaa	gtg Val	gtc Val 55	ctg Leu	agc Ser	atg Met	gaa Glu	cgg Arg 60	gcg Ala	ctg Leu	cgc Arg	tcc Ser	192
cgg Arg 65	gca Ala	gcc Ala	ctc Leu	cgc Arg	gcc Ala 70	ctt Leu	cgc Arg	ctg Leu	cgc Arg	tgc Cys 75	cgc Arg	acc Thr	cag Gln	tgt Cys	gcc Ala 80	240
gcc Ala	gac Asp	ttc Phe	ccg Pro	tgg Trp 85	gag Glu	ctg Leu	gac Asp	ccc Pro	gac Asp 90	tgg Trp	tcc Ser	ccc Pro	agc Ser	ccg Pro 95	gcc Ala	288
cag Gln	gcc Ala	tcg Ser	ggc Gly 100	gcc Ala	gcc Ala	gcc Ala	ctg Leu	cgc Arg 105	gac Asp	ctg Leu	agc Ser	ttc Phe	ttc Phe 110	Gly aaa	ggc Gly	336
ctt Leu	ctg Leu	cgt Arg 115	cgc Arg	gct Ala	gcc Ala	tgc Cys	ctg Leu 120	cgc Arg	cgc Arg	tgc Cys	ctc Leu	999 Gly 125	ccg Pro	ccg Pro	gcc Ala	384
gcc Ala	cac His 130	tcg Ser	ctc Leu	agc Ser	gaa Glu	gag Glu 135	atg Met	gag Glu	ctg Leu	gag Glu	ttc Phe 140	cgc Arg	aag Lys	cgg Arg	agc Ser	432
ccc Pro 145	tac Tyr	aac Asn	tac Tyr	ctg Leu	cag Gln 150	gtc Val	gcc Ala	tac Tyr	ttc Phe	aag Lys 155	gtg Val	cag Gln	acc Thr	tgc Cys	ctg Leu 160	480
gaa Glu	cca Pro	ggc Gly	gj ggc	cgg Arg 165	ggt Gly	cct Pro	tct Ser	Gly 999	gag Glu 170	agg Arg	agt Ser	gtt Val	gca Ala	999 Gly 175	gac Asp	528
ctg Leu	agg Arg	agc Ser	ttg Leu 180	gjà aaa	gat Asp	cgg Arg	gga Gly	agt Ser 185	gtc Val	cgc Arg	agg Arg	gag Glu	999 Gly 190	aaa Lys	gtg Val	576
gcc Ala	tcc Ser	tgg Trp 195	ctg Leu	gly aaa	agc Ser	tct Ser	cct Pro 200	cgg Arg	agc Ser	cgg Arg	gga Gly	gag Glu 205	ctg Leu	ctc Leu	cct Pro	624
Gly	agg Arg 210	aga Arg	cct Pro	tcc Ser	tcg Ser	ccc Pro 215	agt Ser	tcg Ser	cat His	gly aaa	cag Gln 220	atg Met	cta Leu	acc Thr	cca Pro	672
aag Lys 225	atc Ile	aac Asn	aag Lys	ttg Leu	gag Glu 230	aaa Lys	gct Ala	gtt Val	gct Ala	gca Ala 235	gca Ala	cac His	acc Thr	ttc Phe	ttc Phe 240	720
gtg Val	ggc Gly	aat Asn	cct Pro	gag Glu 245	cac His	atg Met	gaa Glu	atg Met	cag Gln 250	cag Gln	aac Asn	cta Leu	gac Asp	tat Tyr 255	tac Tyr	768
caa Gln	acc Thr	atg Met	tct Ser 260	gga Gly	gtg Val	aag Lys	gag Glu	gcc Ala 265	gac Asp	ttc Phe	aag Lys	gat Asp	ctt Leu 270	gag Glu	act Thr	816

					gaa Glu											864
-	_		_	_	gct Ala											912
			-		gag Glu 310		_	-	_		_	_				960
					aac Asn											1008
_			_		tac Tyr		_	_			_	_	_			1056
					tcc Ser											1104
					tat Tyr											1152
385 Gly ggg	aat Asn	tat Tyr	aca Thr	cag Gln	gct Ala 390	gtt Val	gaa Glu	tgt Cys	gcc	aag Lys 395	acc Thr	tat Tyr	ctt Leu	ctc Leu	ttc Phe 400	1200
					gtg Val											1248
					cac His											1296
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gct Ala	tat Tyr 450	Asp	gtt Val	ttt Phe	gga Gly	att Ile 455	ccc Pro	ttt Phe	gtg Val	gat Asp	ccg Pro 460	gat Asp	tca Ser	tgg Trp	act Thr	1392
					ccc Pro 470											1440
cgg Arg	gaa Glu	aca Thr	gcc Ala	gta Val 485	cgc Arg	atc Ile	tcc Ser	cag Gln	gag Glu 490	att Ile	GJÀ aaa	aac Asn	ctt Leu	atg Met 495	aag Lys	1488
gaa Glu	atc Ile	gag Glu	acc Thr 500	Leu	gtg Val	gaa Glu	gag Glu	aag Lys 505	Thr	aag Lys	gag Glu	tca Ser	ctg Leu 510	Asp	gtg Val	1536

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ctc Leu	acc Thr 530	atg Met	aac Asn	tcc Ser	aaa Lys	ctc Leu 535	ctg Leu	aat Asn	ggt	tcc Ser	cag Gln 540	cgg Arg	gtg Val	gtg Val	atg Met	1632
gac Asp 545	ggc ggc	gta Val	atc Ile	tct Ser	gac Asp 550	cac His	gag Glu	tgt Cys	cag Gln	gag Glu 555	ctg Leu	cag Gln	aga Arg	ctg Leu	acc Thr 560	1680
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ctg Leu 625	gat Asp	acg Thr	ccc Pro	ctc Leu	tac Tyr 630	ttt Phe	tcc Ser	tac Tyr	tct Ser	cat His 635	ctg Leu	gtg Val	tgc Cys	cgc Arg	act Thr 640	1920
gcc Ala	atc Ile	gaa Glu	gag Glu	gtc Val 645	cag Gln	gca Ala	gag Glu	agg Arg	aag Lys 650	gat Asp	gat Asp	agt Ser	cat His	cca Pro 655	gtc Val	1968
cac His	gtg Val	gac Asp	aac Asn 660	tgc Cys	atc Ile	ctg Leu	aat Asn	gcc Ala 665	gag Glu	acc Thr	ctc Leu	gtg Val	tgt Cys 670	gtc Val	aaa Lys	2016
gag Glu	ccc Pro	cca Pro 675	gcc Ala	tac Tyr	acc Thr	ttc Phe	cgc Arg 680	gac Asp	tac Tyr	agc Ser	gcc Ala	atc Ile 685	ctt Leu	tac Tyr	cta Leu	2064
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aag Lys 705	acc Thr	gtg Val	acg Thr	gca Ala	gag Glu 710	gtg Val	cag Gln	cct Pro	cag Gln	tgt Cys 715	gga Gly	aga Arg	gcc Ala	gtg V al	gga Gly 720	2160
ttc Phe	tct Ser	tca Ser	ggc	act Thr 725	gaa Glu	aac Asn	cca Pro	cat His	gga Gly 730	gtg Val	aag Lys	gct Ala	gtc Val	acc Thr 735	agg Arg	2208
GJ À aaa	cag Gln	cgc Arg	tgt Cys 740	gcc Ala	atc Ile	gcc Ala	ctg Leu	tgg Trp 745	ttc Phe	acc Thr	ctg Leu	gac Asp	cct Pro 750	cga Arg	cac His	2256
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Ser Glu Arg Asp Arg Val Gln Ala Asp Asp Leu Val Lys Met Leu Phe 755 760 765	
agc cca gaa gag atg gac ctc tcc cag gag cag ccc ctg gat gcc cag Ser Pro Glu Glu Met Asp Leu Ser Gln Glu Gln Pro Leu Asp Ala Gln 770 775 780	2352
cag ggc ccc ccc gaa cct gca caa gag tct ctc tca ggc agt gaa tcg Gln Gly Pro Pro Glu Pro Ala Gln Glu Ser Leu Ser Gly Ser Glu Ser 785 790 795 800	2400
aag ccc aag gat gag cta tga ca gcgtccaggt cagacggatg ggtgactaga Lys Pro Lys Asp Glu Leu 805	2453
cccatggaga ggaactette tgcactetga getggeeage ccctegggge tgcagageag	2513
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acacaggeee ageeaceeee aggggeetee acaggeeget geataacage gatacagtae	2693
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<211> 3000

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)..(2721)

<400> 22

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Val Leu Arg Ser Leu His Ala Ala Gly Leu Leu Gly Pro Ser Leu Arg
20 25 30

gac ccg ctg gac gcg ctg ccc gtg cac cac gcg gcc cgc gct ggg aag 144
Asp Pro Leu Asp Ala Leu Pro Val His His Ala Ala Arg Ala Gly Lys
35 40 45

ctg cac tgt ctg cgc ttc ctg gtg gag gaa gcc gcc ctc ccc gcc gcg
Leu His Cys Leu Arg Phe Leu Val Glu Glu Ala Ala Leu Pro Ala Ala
50
55
60

ggc cac ctc gcc tgc ctg cag tgg ctg ctg tcg cag ggc ggc tgc aga 288
Gly His Leu Ala Cys Leu Gln Trp Leu Leu Ser Gln Gly Gly Cys Arg
85 90 95

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ctg Leu	gtg Val	cca Pro 115	Val	tcc Ser	tgc Cys	cgt Arg	gac Asp 120	Asn	cag Gln	gac Asp	aaa Lys	gac Asp 125	aat Asn	tct Ser	ggt Gly		384
gcc Ala	aca Thr 130	gtc Val	ttg Leu	cat His	ctg Leu	gct Ala 135	gcc Ala	cgc Arg	ttc Phe	Gly	cac His 140	Pro	gag Glu	gtg Val	gtg Val		432
aac Asn 145	tgg Trp	ctc Leu	ttg Leu	cat His	cat His 150	ggc	ggt Gly	gj aaa	gac Asp	ccc Pro 155	acc Thr	gcg Ala	gcc Ala	aca Thr	gac Asp 160		480
atg Met	Gly	gcc Ala	ctg Leu	cct Pro 165	atc Ile	cac His	tac Tyr	gct Ala	gcc Ala 170	gcc Ala	aaa Lys	gga Gly	gac Asp	ttc Phe 175	ccc Pro		528
tcc Ser	ctg Leu	agg Arg	ctt Leu 180	ctc Leu	gtc Val	gag Glu	cac His	tac Tyr 185	cct Pro	gag Glu	gga Gly	gtg Val	aat Asn 190	gcc Ala	caa Gln		576
acc Thr	aag Lys	aac Asn 195	ggt Gly	gcc Ala	acg Thr	ccc Pro	ctg Leu 200	tac Tyr	ctg Leu	gcg Ala	tgc Cys	cag Gln 205	gag Glu	ggc Gly	cac His		624
ctg Leu	gag Glu 210	gtg Val	acc Thr	cag Gln	tac Tyr	ctg Leu 215	gtg Val	cag Gln	gaa Glu	tgc Cys	ggc Gly 220	gca Ala	gac Asp	ccg Pro	cac His		672
gcg Ala 225	cgc Arg	gcc Ala	cac His	gac Asp	ggc Gly 230	atg Met	acc Thr	ccg Pro	ctg Leu	cac His 235	gcc Ala	gcg Ala	gcg Ala	cag Gln	atg Met 240		720
Gly	cac His	agc Ser	cca Pro	gtc Val 245	atc Ile	gtg Val	tgg Trp	ttg Leu	gtg Val 250	agc Ser	tgc Cys	acc Thr	gac Asp	gtg Val 255	agc Ser		768
ctg Leu	tcc Ser	gag Glu	cag Gln 260	gac Asp	aaa Lys	gac Asp	ggc Gly	gcc Ala 265	acc Thr	gcc Ala	atg Met	cac His	ttc Phe 270	gcg Ala	gcg Ala		816
agc Ser	cgc Arg	ggc Gly 275	cac His	acc Thr	aag Lys	gtg Val	ctc Leu 280	agc Ser	tgg Trp	ctg Leu	ctg Leu	ctg Leu 285	cac His	ggc Gly	gly aaä		864
gag Glu	atc Ile 290	tcg Ser	gct Ala	gac Asp	ctg Leu	tgg Trp 295	ggc Gly	GJA aaa	acc Thr	ccg Pro	ctg Leu 300	cac His	gac Asp	gcc Ala	gcc Ala		912
gag Glu 305	aac Asn	gjå aaa	gag Glu	cta Leu	gag Glu 310	tgc Cys	tgc Cys	cag Gln	atc Ile	ctg Leu 315	gta Val	gtg V al	aac Asn	ggc Gly	gcg Ala 320		960
gag Glu	ctg Leu	gac Asp	gtc Val	cgc Arg 325	gac Asp	cgc Arg	gac Asp	ej aaa	tac Tyr 330	acg Thr	gcc Ala	gcc Ala	gac Asp	ctg Leu 335	tcg Ser	1	008

gac Asp	ttc Phe	aac Asn	ggc Gly 340	cac His	agc Ser	cac His	tgc Cys	acc Thr 345	cgc Arg	tac Tyr	ctg Leu	cgc Arg	acg Thr 350	gtg Val	gag Glu	1056
aac Asn	ctg Leu	cac His 355	agg Arg	Gly aaa	atg Met	gtc Val	ctg Leu 360	gct Ala	ctg Leu	G1Å aaa	gct Ala	gca Ala 365	gaa Glu	cac His	agc Ser	1104
aag Lys	gcc Ala 370	cag Gln	agg Arg	cca Pro	gag Glu	gct Ala 375	gca Ala	GJ ^A aaa	gjå aaa	cct Pro	gag Glu 380	gat Asp	gaa Glu	ctt Leu	ccc Pro	1152
ccc Pro 385	gcg Ala	aaa Lys	gag Glu	tct Ser	ctg Leu 390	gaa Glu	gag Glu	aat Asn	gaa Glu	tgg Trp 395	ccc Pro	agc Ser	agg Arg	ggt Gly	cag Gln 400	1200
ggc	ttg Leu	gtg Val	ccc Pro	tca Ser 405	gca Ala	ccc Pro	act Thr	gct Ala	gtt Val 410	ggc Gly	cag Gln	agc Ser	gtg Val	gag Glu 415	cac His	1248
cgc Arg	gtg Val	ctt Leu	tcc Ser 420	cgg Arg	gat Asp	cca Pro	tcc Ser	gca Ala 425	gag Glu	ctg Leu	gag Glu	gct Ala	aag Lys 430	cag Gln	ccg Pro	1296
	tca Ser															1344
aac Asn	ttt Phe 450	gac Asp	ctc Leu	agc Ser	tcg Ser	cct Pro 455	acc Thr	agc Ser	acc Thr	ctc Leu	tcc Ser 460	aac Asn	tac Tyr	gac Asp	tcc Ser	1392
tgc Cys 465	tcc Ser	tcc Ser	agc Ser	cac His	tcc Ser 470	agc Ser	atc Ile	aag Lys	ggc Gly	cag Gln 475	cac His	cct Pro	cca Pro	tgt Cys	999 Gly 480	1440
	tcc Ser															1488
aac Asn	ccg Pro	gag Glu	ctg Leu 500	ggc ggc	ctg Leu	cct Pro	cgg Arg	ggc Gly 505	acg Thr	att Ile	eja aaa	aag Lys	ccc Pro 510	aca Thr	ccc Pro	1536
cca Pro	cca Pro	ccc Pro 515	cca Pro	ccc Pro	agc Ser	ttc Phe	ccc Pro 520	ccg Pro	cca Pro	ccc Pro	ccg Pro	ccc Pro 525	cca Pro	ggc ggc	acc Thr	1584
caa Gln	ctg Leu 530	ccc Pro	cca Pro	ccc Pro	cca Pro	cct Pro 535	Gly ggc	tac Tyr	cca Pro	gct Ala	ccc Pro 540	aag Lys	cct Pro	cct Pro	gta Val	1632
gga Gly 545	cca Pro	cag Gln	gca Ala	gct Ala	gac Asp 550	atc Ile	tac Tyr	atg Met	cag Gln	acc Thr 555	aag Lys	aac Asn	aaa Lys	ctc Leu	cgc Arg 560	1680
cac His	gtg Val	gag Glu	aca Thr	gag Glu 565	gcc Ala	ctc Leu	aag Lys	aag Lys	gag Glu 570	ctg Leu	agc Ser	tcc Ser	tgt Cys	gac Asp 575	ggc Gly	1728
cac	gac	aaa	ctg	cgg	agg	cag	gac	tcc	agc	cgc	aag	ccc	cgc	gcc	ttc	1776

His	Asp	Gly	Leu 580	Arg	Arg	Gln	Asp	Ser 585	Ser	Arg	Гув	Pro	Arg 590	Ala	Phe	
agc Ser	aag Lys	cag Gln 595	ccc Pro	agc Ser	acg Thr	gjå aaa	gac Asp 600	tac Tyr	tac Tyr	cgg Arg	cag Gln	ctg Leu 605	ggc Gly	cgc Arg	tgc Cys	1824
ccc Pro	ggc Gly 610	gag Glu	acg Thr	ctg Leu	gcc Ala	gca Ala 615	cgc Arg	ccg Pro	ggc ggc	atg Met	gcg Ala 620	cac His	agc Ser	gag Glu	gag Glu	1872
gcg Ala 625	gcg Ala	ctg Leu	ctt Leu	cct Pro	630 Gl ^à 333	aac Asn	cat His	gtt Val	cct Pro	aac Asn 635	ggc Gly	tgc Cys	gcc Ala	gcg Ala	gac Asp 640	1920
	aag Lys															1968
	ctg Leu															2016
ctc Leu	gag Glu	agc Ser 675	gct Ala	ggc Gly	cct Pro	ggc	tgc Cys 680	gjå aaa	cag Gln	cgc Arg	cgc Arg	tcc Ser 685	tcc Ser	tcg Ser	tcc Ser	2064
acc Thr	ggc Gly 690	agc Ser	acc Thr	aag Lys	tct Ser	ttc Phe 695	aac Asn	atg Met	atg Met	tcc Ser	ccg Pro 700	acg Thr	ggc Gly	gac Asp	aac Asn	2112
	gag Glu		_	_			_	_		_	_	_	_	_	_	2160
	cag Gln															2208
gcc Ala	ttc Phe	cag Gln	ccc Pro 740	gat Asp	tcg Ser	ccg Pro	ctg Leu	cct Pro 745	tct Ser	gtg Val	tca Ser	cct Pro	gca Ala 750	ctg Leu	tca Ser	2256
	gtc Val															2304
aat Asn	gga Gly 770	agc Ser	ttg Leu	gtt Val	ccc Pro	gtg Val 775	ccg Pro	ccc Pro	act Thr	act Thr	cct Pro 780	gcg Ala	ccg Pro	gga Gly	gtg Val	2352
cag Gln 785	ctg Leu	gac Asp	gtg Val	gag Glu	gct Ala 790	ct <i>c</i> Leu	atc Ile	ccc Pro	acg Thr	cac His 795	gat Asp	gag Glu	cag Gln	Gly ggc	cgg Arg 800	2400
ccc Pro	atc Ile	ccc Pro	gag Glu	tgg Trp 805	aag Lys	cgc Arg	cag Gln	gtg Val	atg Met 810	gtg Val	cgc Arg	aag Lys	atg Met	cag Gln 815	ctg Leu	2448
aag Lys	atg Met	cag Gln	gag Glu	gag Glu	gag Glu	gag Glu	cag Gln	agg Arg	cgg Arg	aag Lys	gag Glu	gag Glu	gag Glu	gag Glu	gag Glu	2496

830

820

	020	023		
	gcc agc atg ccc gcc Ala Ser Met Pro Ala 840		gac ctc ctg cgg aag Asp Leu Leu Arg Lys 845	2544
	gaa gag agg gag cag Glu Glu Arg Glu Gln 855			2592
	gag ctg cgg cgg gag Glu Leu Arg Arg Glu 870			2640
	tac gat gag agc aag Tyr Asp Glu Ser Lys 885			2688
	aag ggg gac atc gct Lys Gly Asp Ile Ala 900	_	aggeegea gaeteetgte	2739
cgcagcctcg (cagctccgtg gggccctcc	g ccccagcccc	agccagccag gccctggtgg	2799
aaaggctggg a	agccgcacag ccctcccct	c ctgcgctgga	aaccctccct gacccccacc	2859
ctggcccccc (gtatececag ceettggea	a cactggagtg	cacacgccgc cacggttgcc	2919
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gco Ala 65	Arg	gcc Ala	egc Arg	aac Asn	ggc Gly 70	Ala	aca Thr	ccg Pro	gcc Ala	cac His	Asp	gcc Ala	tco Ser	gcc Ala	acc Thr 80		240
Gly	cac His	ctc Leu	gcc Ala	tgc Cys 85	Leu	cag Gln	tgg Trp	ctg Leu	ctg Leu 90	tcg Ser	cag Gln	ggc	Gly	tgc Cys 95	Arg		288
gtg Val	cag Gln	gca Ala	ttc Phe 100	cct Pro	gag Glu	tcc Ser	ctg Leu	gga Gly 105	gtc Val	agg Arg	gct Ala	gtg Val	gcc Ala 110	Leu	ggc		336
ctg Leu	gtg Val	cca Pro 115	Val	tcc Ser	tgc Cys	cgt Arg	gac Asp 120	aac Asn	cag Gln	gac Asp	aaa Lys	gac Asp 125	aat Asn	tct Ser	ggt Gly		384
gcc Ala	aca Thr 130	gtc Val	ttg Leu	cat His	ctg Leu	gct Ala 135	gcc Ala	cgc Arg	ttc Phe	ggc	cac His 140	ccc Pro	gag Glu	gtg Val	gtg Val		432
aac Asn 145	tgg Trp	ctc Leu	ttg Leu	cat His	cat His 150	ggc	ggt Gly	GJ A aaa	gac Asp	ccc Pro 155	acc Thr	gcg Ala	gcc Ala	aca Thr	gac Asp 160		480
atg Met	ggc	gcc Ala	ctg Leu	cct Pro 165	atc Ile	cac His	tac Tyr	gct Ala	gcc Ala 170	gcc Ala	aaa Lys	gga Gly	gac Asp	ttc Phe 175	ccc Pro		528
tcc Ser	ctg Leu	agg Arg	ctt Leu 180	ctc Leu	gtc Val	gag Glu	cac His	tac Tyr 185	cct Pro	gag Glu	gga Gly	gtg Val	aat Asn 190	gcc Ala	caa Gln		576
acc Thr	aag Lys	aac Asn 195	ggt Gly	gcc Ala	acg Thr	ccc Pro	ctg Leu 200	tac Tyr	ctg Leu	gcg Ala	tgc Cys	cag Gln 205	gag Glu	Gly	cac His		624
ctg Leu	gag Glu 210	gtg Val	acc Thr	cag Gln	tac Tyr	ctg Leu 215	gtg Val	cag Gln	gaa Glu	tgc Cys	ggc Gly 220	gca Ala	gac Asp	ccg Pro	cac His		672
gcg Ala 225	cgc Arg	gcc Ala	cac His	gac Asp	ggc Gly 230	atg Met	acc Thr	ccg Pro	ctg Leu	cac His 235	gcc Ala	gcg Ala	gcg Ala	cag Gln	atg Met 240	•	720
ggc	cac His	agc Ser	cca Pro	gtc Val 245	atc Ile	gtg Val	tgg Trp	ttg Leu	gtg Val 250	agc Ser	tgc Cys	acc Thr	gac Asp	gtg Val 255	agc Ser		768
ctg Leu	tcc Ser	gag Glu	cag Gln 260	Asp Asp	aaa Lys	gac Asp	Gly	gcc Ala 265	acc Thr	gcc Ala	atg Met	cac His	ttc Phe 270	gcg Ala	gcg Ala		816
agc Ser	cgc Arg	ggc Gly 275	cac His	acc Thr	aag Lys	gtg Val	ctc Leu 280	agc Ser	tgg Trp	ctg Leu	ctg Leu	ctg Leu 285	cac His	ggc Gly	Gly aaa		864
gag Glu	atc Ile 290	tcg Ser	gct Ala	gac Asp	ctg Leu	tgg Trp 295	ggc Gly	gjà aaa	acc Thr	ccg Pro	ctg Leu 300	cac His	gac Asp	gcc Ala	gcc Ala		912
gag	aac	9 99	gag	cta	gag	tgc	tgc	cag	atc	ctg	gta	gtg	aac	ggc	gcg		960

Glu 305	Asn	Gly	Glu	Leu	Glu 310	Сув	Cys	Gln	Ile	Leu 315	Val	Val	Asn	Gly	Ala 320	
	ctg Leu	_	_	_	_	_	_			-	_	_	_	_	-	1008
	ttc Phe				_		_		_		_	_	_			1056
aac Asn	ctg Leu	agc Ser 355	gtg Val	gag Glu	cac His	cgc Arg	gtg Val 360	ctt Leu	tcc Ser	cgg Arg	gat Asp	cca Pro 365	tcc Ser	gca Ala	gag Glu	1104
	gag Glu 370															1152
	tcg Ser															1200
	tcc Ser			_		_			_			_		_		1248
	cac His															1296
	tac Tyr															1344
	999 Gly 450	_									_			_		1392
	ccg Pro						_									1440
	ccc Pro															1488
acc Thr	aag Lys	aac Asn	aaa Lys 500	ctc Leu	cgc Arg	cac His	gtg Val	gag Glu 505	aca Thr	gag Glu	gcc Ala	ctc Leu	aag Lys 510	aag Lys	gag Glu	1536
ctg Leu	agc Ser	tcc Ser 515	tgt Cys	gac Asp	Gly	cac His	gac Asp 520	GJÀ aaa	ctg Leu	cgg Arg	agg Arg	cag Gln 525	gac Asp	tcc Ser	agc Ser	1584
_	aag Lys 530			_		_	_	_		_	_		_			1632
	cag Gln															1680

545	550	555		560
atg gcg cac agc ga Met Ala His Ser Gl 56	u Glu Ala Ala			
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ccc cca ccg ccg cc Pro Pro Pro Pro Pr 595	g ccg ccc ctg o Pro Pro Leu 600	ccg gag gcc g Pro Glu Ala A	cg agt tcg cca la Ser Ser Pro 605	ccg 1824 Pro
ccg gcc ccg cct ct Pro Ala Pro Pro Le 610	g ccc ctc gag u Pro Leu Glu 615	Ser Ala Gly P	ct ggc tgc ggg Pro Gly Cys Gly	cag 1872 Gln
ege ege tee tee te Arg Arg Ser Ser Se 625				
tcc ccg acg ggc ga Ser Pro Thr Gly As 64	p Asn Ser Glu			
aag agc ctg aag co Lys Ser Leu Lys Pr 660	-			
tca ggc atc ggg ca Ser Gly Ile Gly Gl 675				
gtg tca cct gca ct Val Ser Pro Ala Le 690		Arg Ser Pro T		
ggg ttt cag ccg ct Gly Phe Gln Pro Le 705				
act cct gcg ccg gg Thr Pro Ala Pro GJ 72	y Val Gln Leu	gac gtg gag g Asp Val Glu A 730	gct ctc atc ccc Ala Leu Ile Pro 735	acg 2208 Thr
cac gat gag cag go His Asp Glu Gln Gl 740	c cgg ccc atc y Arg Pro Ile	ccc gag tgg a Pro Glu Trp L 745	ag cgc cag gtg ys Arg Gln Val 750	atg 2256 Met
gtg cgc aag atg ca Val Arg Lys Met Gl 755	g ctg aag atg n Leu Lys Met 760	cag gag gag g Gln Glu Glu G	gag gag cag agg Blu Glu Gln Arg 765	cgg 2304 Arg
aag gag gag gag ga Lys Glu Glu Glu Gl 770		Leu Ala Ser M		
cgg gac ctc ctg co Arg Asp Leu Leu Ar 785				

			gag Glu													2	2448
			aag Lys 820													2	2496
			cga Arg													2	2544
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gto Val 99	acc L Thr	atc Ile	agc Ser	cct Pro	gtg Val 100	cag Gln	ccc Pro	gag Glu	gag Glu	cgg Arg 105	cgg Arg	ctc Leu	agg Arg	gcg Ala	gcc Ala 110	518
	cgg Arg															566
gct Ala	ggg Gly	gcc Ala	gag Glu 130	cct Pro	agc Ser	aca Thr	gaa Glu	gcc Ala 135	cca Pro	agg Arg	tgg Trp	ccc Pro	ctg Leu 140	cct Pro	gtg Val	614
	g agg s Arg															662
	gct Ala 160															710
	g agt / Ser															758
tca Ser	ctg Leu	ccc Pro	ccc Pro	aca Thr 195	ggc	act Thr	gag Glu	gcc Ala	act Thr 200	gcc Ala	agc Ser	act Thr	gjå aaa	gtg Val 205	gca Ala	806
	tgc Cys															854
	. Gly															902
	gtg Val 240															950
	tca Ser															998
	gct Ala															1046
	tgt Cys															1094
	c cca Pro															1142
gtg Val	acc Thr 320	ctg Leu	gag Glu	ctg Leu	acc Thr	aag Lys 325	gjà aaa	GJA aaa	agg Arg	cag Gln	gca Ala 330	aac Asn	caa Gln	acc Thr	ttc Phe	1190
ttt	ttt	tta	ctg	cag	gcc	gtg	agg	cta	ggc	agg	tgt	tca	gat	gag	gtg	1238

Phe 335	Phe	Leu	Leu	Gln	Ala 340	Val	Arg	Leu	Gly	Arg 345	Cys	Ser	qaA	Glu	Val 350	
	_	_		_	gcc Ala		_			_			_	_		1286
		-	_		ctc Leu	-			_	-	_		_			1334
					cag Gln		_			_	_		-		_	1382
_	_	_	_		cct Pro		_	-	_		_	_	_	_	_	1430
	_	_	_		ctt Leu 420			_	_		_	_		_	_	1478
				_	gtg Val				-				-	_		1526
					gag Glu											1574
					act Thr											1622
_	-				cag Gln			-		_	_	_				1670
					tcc Ser 500											1718
tgt Cys	gtg Val	gag Glu	att Ile	tct Ser 515	ctg Leu	ggc Gly	cgt Arg	gtg Val	ttt Phe 520	gcc Ala	agt Ser	ggc Gly	cag Gln	gcc Ala 525	tat Tyr	1766
					gcc Ala											1814
ttt Phe	gac Asp	ccc Pro 545	atg Met	gcg Ala	gtt Val	cgc Arg	tgt Cys 550	gac Asp	ccc Pro	cgt Arg	gtg Val	ctg Leu 555	cac His	ttc Phe	tat Tyr	1862
					Gly											1910
gat Asp	gag Glu	gca Ala	gcc Ala	tca Ser	gac Asp	cag Gln	gag Glu	aac Asn	atg Met	gac Asp	cca Pro	atc Ile	ctc Leu	tga	gcc	1958

585

2632

60

580

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575

<211> 1769

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (189)..(1769)

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gteggcacaa accagcagag geggtgacga tgeteteggg catagaggeg geggcagggg

ttc Phe	ctg Leu	cgc Arg 65	aca Thr	ttg Leu	cgc Arg	ctc Leu	aag Lys 70	ctg Leu	gct Ala	gcg Ala	gcc Ala	ccg Pro 75	ggt Gly	ccc Pro	Gly 939	422
ccg Pro	gcc Ala 80	tcc Ser	gcc Ala	cga Arg	gcg Ala	cag Gln 85	ctg Leu	ctg Leu	Gly ggc	ccg Pro	cgg Arg 90	ccc Pro	cgc Arg	gac Asp	ttc Phe	470
gtc Val 95	acc Thr	atc Ile	agc Ser	cct Pro	gtg Val 100	cag Gln	ccc Pro	gag Glu	gag Glu	cgg Arg 105	cgg Arg	ctc Leu	agg Arg	gcg Ala	gcc Ala 110	518
acc Thr	cgg Arg	gtt Val	ccg Pro	gac Asp 115	act Thr	acg Thr	ctg Leu	gtg Val	aag Lys 120	cgg Arg	cct Pro	gtg Val	gag Glu	ccc Pro 125	cag Gln	566
gct Ala	GJÀ aaa	gcc Ala	gag Glu 130	cct Pro	agc Ser	aca Thr	gaa Glu	gcc Ala 135	cca Pro	agg Arg	tgg Trp	ccc Pro	ctg Leu 140	cct Pro	gtg Val	614
aag Lys	agg Arg	ctg Leu 145	agc Ser	ttg Leu	ccc Pro	tcc Ser	acc Thr 150	aag Lys	cca Pro	cag Gln	ctt Leu	tct Ser 155	gag Glu	gaa Glu	cag Gln	662
gct Ala	gct Ala 160	gtg Val	ctg Leu	agg Arg	gcc Ala	gcc Ala 165	ctg Leu	aaa Lys	ggc ggc	cag Gln	agc Ser 170	atc Ile	ttc Phe	ttc Phe	act Thr	710
			gga Gly													758
			ccc Pro													806
-			atc Ile 210							_		_				854
			gct Ala													902
			cag Gln													950
			gtg Vál													998
			cgg Arg													1046
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999 Gly 415	gtg Val	gta Val	gtt Val	G1 y 999	ttc Phe 420	gag Glu	gca Ala	gaa Glu	gjà aaa	aga Arg 425	Gly 333	cta Leu	ccc Pro	cag Gln	gtg Val 430	1478
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gat Asp	gat Asp	gat Asp	gag Glu	gca Ala 515	gcc Ala	tca Ser	gac Asp	cag Gln	gag Glu 520	aac Asn	atg Met	gac Asp	cca Pro	atc Ile 525	ctc Leu	1766
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Val	Thr	Asn 195	Thr	Ala	Arg	Thr	Суs 200		Thr	Phe	Ser	Ala 205		Val	Gly	
gag Glu	tca Ser 210	gct Ala	act Thr	gca Ala	aaa Lys	ttc Phe 215	cat His	gtc Val	aca Thr	cca Pro	ttg Leu 220	Phe	gga Gly	aat Asn	gtc Val	672
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tat Tyr	ggt Gly	ggt Gly	gta Val	aaa Lys 325	aag Lys	tct Ser	cta Leu	gga Gly	gct Ala 330	agt Ser	aga Arg	tcc Ser	cga Arg	999 Gly 335	ata Ile	1008
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gaa Glu	gat Asp	att Ile	gca Ala	gga Gly 405	gta Val	gaa Glu	ttt Phe	gct Ala	aaa Lys 410	gcc Ala	acc Thr	ata Ile	aag Lys	gaa Glu 415	ata Ile	1248
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ccc Pro	cct Pro	aaa Lys	gga Gly	att Ile	ttg Leu	ctc Leu	ttt Phe	ggt Gly	cct Pro	cct Pro	G1A aaa	act Thr	ggt Gly	aaa Lys	act Thr	1344

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gat Asp	gga Gly 530	gca Ala	aca Thr	aca Thr	tct Ser	tct Ser 535	gaa Glu	gat Asp	cgt Arg	atc Ile	cta Leu 540	gtg Val	gtg Val	gga Gly	gca Ala	1632
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gta Val	att Ile	aat Asn	cta Leu 580	atg Met	tcc Ser	aaa Lys	gag Glu	cag Gln 585	tgt Cys	tgc Cys	ctc Leu	agt Ser	gaa Glu 590	gaa Glu	gaa Glu	1776
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aca Thr	cag Gln 610	ctt Leu	tgc Cys	agg Arg	gag Glu	gct Ala 615	tct Ser	ctt Leu	ggt Gly	cct Pro	att Ile 620	cgc Arg	agt Ser	tta Leu	caa Gln	1872
act Thr 625	gct Ala	gac Asp	att Ile	gct Ala	acc Thr 630	ata Ile	aca Thr	ccg Pro	gat Asp	caa Gln 635	gtt Val	cga Arg	ccc Pro	ata Ile	gct Ala 640	1920
tac Tyr	att Ile	gat Asp	ttt Phe	gaa Glu 645	aat Asn	gct Ala	ttt Phe	aga Arg	act Thr 650	gtg Val	cga Arg	cct Pro	agt Ser	gtt Val 655	tct Ser	1968
cca Pro	aaa Lys	gat Asp	tta Leu 660	gag Glu	ctt Leu	tat Tyr	gaa Glu	aac Asn 665	tgg Trp	aac Asn	aaa Lys	act Thr	ttt Phe 670	ggt Gly	tgt Cys	2016
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tgaa	aac														a ata	228
			: Asr l	ı Leı	ı Sei		ı Val	l Let	ı Ala	a Ala	a Phe		s Lev	ı Gly	y Ile	
acc	tcc	act	at t	003	222	+++	~ 2~	a aa	22+	++~	~>+	202	226	+~~	toa	276
	Ser															270
15				110	20	1110			11011	25			- 75		30	
cag	tgg	aaq	qca	aca	cac	aga	aga	tta	tat	qqc	qcq	aat	qaa	qaa	gga	324
	Trp															
	_	_		35			_		40	-				45	-	
tgg	agg	aga	gca	gtg	tgg	gaa	aag	aat	atg	aaa	atg	att	gaa	ctg	cac	372
Trp	Arg	Arg	Ala	Val	\mathtt{Trp}	Glu	Lys	Asn	Met	Lys	Met	Ile	Glu	Leu	His	
			50					55					60			
	ggg	_		_					_			_	_	_		420
Asn	Gly		Tyr	Ser	Gln	Gly		His	Ser	Phe	Thr		Ala	Met	Asn	
		65					70					75				•
	ttt															468
Ala	Phe	Gly	Asp	Met	Thr		Glu	Glu	Phe	Arg		Val	Met	Asn	Gly	
	80					85					90					
	caa															516
	Gln	Tyr	Gln	Lys		Arg	Lys	Gly	Lys		Phe	Gln	Glu	Arg	Leu	
95					100					105					110	
ctt	ctt	gag	atc	ccc	aca	tct	gtg	gac	tgg	aga	gag	aaa	ggc	tac	atg	564
Leu	Leu	Glu	Ile		Thr	Ser	Val	Asp	_	Arg	Glu	Lys	Gly	Tyr	Met	
				115					120					125		
act	cct	gtg	aag	gat	cag	ggt	cag	tgt	ggc	tct	tgt	tgg	gct	ttt	agt	612
Thr	Pro	Val		Asp	Gln	Gly	Gln		Gly	Ser	Сув	\mathtt{Trp}		Phe	Ser	
			130					135					140			
gca	act	ggt	gct	ctg	gaa	aaa	cag	atg	ttc	tgg	aaa	aca	ggc	aaa	ctt	660
Ala	Thr		Ala	Leu	Glu	Gly		Met	Phe	Trp	Гуs	Thr	Gly	Lys	Leu	
		145					150					155				

atc Ile																708
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cag Gln																804
aca Thr																852
acc Thr	ggc Gly	ttt Phe 225	gtg Val	gac Asp	atc Ile	cct Pro	aag Lys 230	cag Gln	gag Glu	aag Lys	gcc Ala	ctg Leu 235	atg Met	aag Lys	gca Ala	900
gtt Val																948
tcc Ser 255																996
agt Ser																1044
agc Ser																1092
ggt Gly	_	-			_				_	_	_	_		_	~~	1140
aga Arg															tga	1188
gctg	gtgg	gac <u>c</u>	ggtga	atgag	gg aa	aggad	ettga	a cts	39gg	tgg	cgca	atgca	atg g	ggagg	gaattc	1248
atct	tcaç	gtc t	acca	agcco	ee eg	gctgt	gtc	g gat	acad	act	cgaa	tcat	tg a	agat	ccgag	1308
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ctat	aaat	ag g	gttta	atatt	a tt	gatt	cact	tac	ctgad	ttt	gcat	tttc	egt t	ttta	aaagg	1428
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	aag Lys															793
	tac Tyr															841
gag Glu	ggg Gly 240	gct Ala	gag Glu	atc Ile	gag Glu	gag Glu 245	ttc Phe	ctg Leu	cgg Arg	cgg Arg	ctg Leu 250	ctg Leu	aag Lys	cgg Arg	ccg Pro	889
	ctg Leu															937
	gcc Ala															985
_	aca Thr	_	_	_		_	_			_						1033
	aca Thr															1081
	ctg Leu 320															1129
	ttc Phe															1177
	cac His															1225
	gag Glu															1273
	cgc Arg															1321
	atc Ile 400															1369
	gtc Val															1417
	atc Ile															1465

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aag Lys	cag Gln	atc Ile	tcc Ser 530	ccg Pro	gag Glu	ctg Leu	tcg Ser	gcc Ala 535	ctg Leu	gct Ala	gtg Val	tac Tyr	tgc Cys 540	cac His	gcc Ala	1	1753
acc Thr	cgc Arg	ctg Leu 545	cgg Arg	acc Thr	ctg Leu	cac His	cct Pro 550	gcc Ala	ccc Pro	aac Asn	gcc Ala	cca Pro 555	caa Gln	ccc Pro	tgc Cys	. 1	1801
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tac Tyr	ccg Pro	ctg Leu	GJÀ 333	ctg Leu 595	cgg Arg	atg Met	aac Asn	tca Ser	gcc Ala 600	aac Asn	tac Tyr	agt Ser	ccc Pro	cag Gln 605	gag Glu	1	945
atg Met	tgg Trp	aac Asn	ser 610	Gly	tgt Cys	cag Gln	ctg Leu	gtg Val 615	gcc Ala	ttg Leu	aac Asn	ttc Phe	cag Gln 620	acg Thr	cca Pro	1	.993
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gtg Val	ctg Leu	act Thr	gca Ala	cag Gln 675	cag Gln	ctg Leu	ccc Pro	aag Lys	ctg Leu 680	aat Asn	gcc Ala	gag Glu	aag Lys	cca Pro 685	cac His	2	185
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Ser Ile Val	Asp Pro 1 690	ieu Val Arg	J Ile Glu 695	Ile His	Gly Val 700	Pro Ala	
gac tgt gcc Asp Cys Ala 705	Arg Gln (Tyr Val				2281
ccc cgc tgg Pro Arg Trp 720			_				2329
gca ctg gtc Ala Leu Val 735	Arg Phe						2377
gac ttt gtg Asp Phe Val							2425
tac cgc cac Tyr Arg His						Ser Pro	2473
gcc acg ctc Ala Thr Leu 785	Phe Ile	_	g Ile Gln	_	tga ggg	cccacct	2522
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											ctc Leu					717
											tcc Ser 175					765
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gaa Glu	aca Thr	Ser	gtg Val 215	gtt Val	gtc Val	cga Arg	gcg Ala	gga Gly 220	gcc Ala	ctc Leu	agc Ser	aat Asn	gtg Val 225	tcc Ser	gtc Val	909
tcc Ser	atc Ile	cag Gln 230	aat Asn	ctc Leu	ctc Leu	ttg Leu	agc Ser 235	cag Gln	aag Lys	aaa Lys	gag Glu	ttg Leu 240	gtg Val	gtc Val	cag Gln	957
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gtg Val 260	tac Tyr	ata Ile	cac His	att Ile	ggc Gly 265	cca Pro	aag Lys	gca Ala	gtc Val	tat Tyr 270	aaa Lys	gag Glu	aca Thr	atg Met	gta Val 275	1053
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acc Thr	atg Met 30	Leu	acg Thr	GJ Y 333	att Ile	gca Ala 35	gtt Val	gga Gly	gcc Ala	ctc Leu	ctg Leu 40	gcc Ala	ctg Leu	gcc Ala	ttg Leu	385
gtt Val 45	ggt Gly	gtc Val	ctc Leu	atc Ile	ctt Leu 50	ttc Phe	atg Met	ttc Phe	aga Arg	agg Arg 55	ctt Leu	aga Arg	caa Gln	ttt Phe	cga Arg 60	433
caa Gln	gca Ala	cag Gln	ccc Pro	act Thr 65	cct Pro	cag Gln	tac Tyr	cgg Arg	ttc Phe 70	cgg Arg	aag Lys	aga Arg	gac Asp	aaa Lys 75	gtg Val	481
atg Met	ttt Phe	tac Tyr	ggc Gly 80	cgg Arg	aag Lys	atc Ile	atg Met	agg Arg 85	aag Lys	gtg Val	acc Thr	aca Thr	ctc Leu 90	ccc Pro	aac Asn	529
acc Thr	ctt Leu	gtg Val 95	gag Glu	aac Asn	act Thr	gcc Ala	ctg Leu 100	ccc Pro	cgg Arg	cag Gln	cgg Arg	gcc Ala 105	agg Arg	aag Lys	agg Arg	577
acc Thr	aag Lys 110	gtg Val	ctg Leu	tct Ser	ttg Leu	gcc Ala 115	aag Lys	agg Arg	att Ile	ctg Leu	cgt Arg 120	ttc Phe	aag Lys	aag Lys	gaa Glu	625
tac Tyr 125	ccg Pro	gcc Ala	ctg Leu	cag Gln	ccc Pro 130	aag Lys	gag Glu	ccc Pro	ccg Pro	ccc Pro 135	tcc Ser	ctg Leu	ctg Leu	gag Glu	gcc Ala 140	673
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ctg Leu	ttc Phe	ctg Leu 175	gag Glu	ctt Leu	tgc Cys	aaa Lys	cac His 180	atc Ile	gtc Val	ttt Phe	gtg Val	cag Gln 185	ctg Leu	cag Gln	gaa Glu	817
GJÀ aaa	gag Glu 190	cac His	gtc Val	ttc Phe	cag Gln	ccc Pro 195	agg Arg	gag Glu	ccg Pro	gac Asp	ccc Pro 200	agc Ser	atc Ile	tgt Cys	gtg Val	865
gtg Val 205	cag Gln	gac Asp	gjå aaa	cgg Arg	ctg Leu 210	gag Glu	gtc Val	tgc Cys	atc Ile	cag Gln 215	gac Asp	act Thr	gac Asp	ggc Gly	acc Thr 220	913
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ctc Leu	agc Ser	atc Ile	ctg Leu 240	gac Asp	atc Ile	atc Ile	acc Thr	ggc Gly 245	cat His	gct Ala	gca Ala	cct Pro	tac Tyr 250	aaa Lys	acg Thr	1009
gtc Val	tcc Ser	gtc Val 255	cgc Arg	gcg Ala	gcc Ala	atc Ile	ccg Pro 260	tcc Ser	acc Thr	atc Ile	ctc Leu	cgg Arg 265	ctt Leu	cca Pro	gct Ala	1057
gcg	gct	ttt	cat	gga	gtt	ttt	gag	aaa	tat	ccg	gaa	act	ctg	gtg	agg	1105

•••	02/4	4340													P	C1/US01/	47004
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	ctg Leu	cac His	aac Asn	tac Tyr	ctc Leu 305	ggc	ctg Leu	acc Thr	aca Thr	gag Glu 310	ctc Leu	ttc Phe	aac Asn	gct Ala	gag Glu 315	agc Ser	1201
	cag Gln	gcc Ala	atc Ile	cct Pro 320	ctc Leu	gtg Val	tct Ser	gta Val	gcc Ala 325	agt Ser	gtg Val	gct Ala	gcc Ala	330 GJA 333	aag Lys	gcc Ala	1249
	aag Lys	aag Lys	cag Gln 335	gtg Val	ttc Phe	tat Tyr	Gly ggc	gaa Glu 340	gaa Glu	gag Glu	cgg Arg	ctt Leu	aaa Lys 345	aag Lys	cca Pro	ccg Pro	1297
	cgg Arg	ctc Leu 350	cag Gln	gag Glu	tcc Ser	tgt Cys	gac Asp 355	tca Ser	ggt Gly	act Thr	gtc Val	ctg Leu 360	cac His	caa Gln	gga Gly	gjå aaa	1345
	caa Gln 365	tgt Cys	cca Pro	gcc Ala	cca Pro	gag Glu 370	tcc Ser	G1 <i>A</i> aaa	gga Gly	tcc Ser	tgc Cys 375	tcc Ser	cac His	tgc Cys	ctc Leu	agg Arg 380	1393
	tca Ser	ccc Pro	cag Gln	gtc Val	atc Ile 385	ttg Leu	cac His	atg Met	cct Pro	gag Glu 390	gcc Ala	acc Thr	aca Thr	cac His	atc Ile 395	ccc Pro	1441
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													gtc Val 425				1537
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	ggt Gly 445	ctc Leu	atc Ile	aga Arg	tgg Trp	ccc Pro 450	ccc Pro	agg Arg	tct Ser	cct Pro	cac His 455	gtg Val	tcc Ser	cca Pro	tct Ser	cct Pro 460	1633
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	gcc Ala	cat His	ctc Leu	ctc Leu 480	aca Thr	tgt Cys	gjå aaa	ctg Leu	gat Asp 485	gtc Val	ctc Leu	aaa Lys	cct Pro	cca Pro 490	acg Thr	gtc Val	1729
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													tcc Ser				1825

510	515	520	
Pro Leu Gly Gln Val P:	ect ggt ggg gag tgg gcc Pro Gly Gly Glu Trp Ala 530 535	tcc cgc gat ggg ctc Ser Arg Asp Gly Leu 540	1873
tca ccc gct gtt ctg as Ser Pro Ala Val Leu So 545	agt gct aac cgg ggg gcc Ser Ala Asn Arg Gly Ala 550	tga atct gaggaggaag	1923
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680

ggg cag ggg ccc atg ccc agg gtc aga tac tat gca ggg gat gaa cgt

Gly Gln Gly Pro Met Pro Arg Val Arg Tyr Tyr Ala Gly Asp Glu Arg

J 02/4	4340								•					r	C 1/U	501/4/004
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ctg Leu	ctc Leu	ctg Leu	agt Ser 70	ggt Gly	gat Asp	gga Gly	aat Asn	act Thr 75	ctc Leu	tac Tyr	gtg Val	Gly aaa	gct Ala 80	cga Arg	gaa Glu	776
gcc Ala	att Ile	ctg Leu 85	gcc Ala	ttg Leu	gat Asp	atc Ile	cag Gln 90	gat Asp	cca Pro	gjà aaa	gtc Val	ccc Pro 95	agg Arg	cta Leu	aag Lys	824
	atg Met 100															872
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	gtt Val															968
	agc Ser														ttg Leu	1016
	atc Ile															1064
	ccc Pro 180															1112
	ggt Gly															1160
	ctg Leu															1208
	cat His							_	_			_		_	_	1256
	tac Tyr															1304
	ctc Leu 260															1352
	gaa Glu				-	-	_					_	_	_	_	1400
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Leu Leu Cys Thr Gln Pro Gly Gln Leu Pro Phe Asn Val Ile Arg His 295 300 305	
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<211> 806

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (487)..(648)

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gcttggatca	aggttaaaag	gccggttgtg	gccttcttgg	tggaagaaag	agagagataa	738
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cca gct gtg gtc tgt gcc cac tgg ggc ccg tgc ctc cgc acg gct ggc
Pro Ala Val Val Cys Ala His Trp Gly Pro Cys Leu Arg Thr Ala Gly
10 15 20 25

cgc gcc agg ctg gtc tgc gtg gcc atc tgg acc ttg gtg ctg ctg cag
Arg Ala Arg Leu Val Cys Val Ala Ile Trp Thr Leu Val Leu Gln
30 35 40

acg atg ccc ttg ctc ttg atg ccc atg acc aag ccg ctg gtg ggc aag

Thr Met Pro Leu Leu Met Pro Met Thr Lys Pro Leu Val Gly Lys

45 50 55

ctg gcc tgc atg gag tac agc atg gag tca gtc ctc ggg ctg ccc
Leu Ala Cys Met Glu Tyr Ser Ser Met Glu Ser Val Leu Gly Leu Pro
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Leu Met Val Leu Val Ala Phe Ala Ile Gly Phe Cys Gly Pro Val Gly 75 80 85	950
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gct ggg aga acc cag tga ccagcg ggaaaggaca ccaccggcgg ggcagcccgg Ala Gly Arg Thr Gln 110	1052
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<220>

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cat cca ege etg tac cae gge tge tat ggg gae ate atg ace atg aag 442

His	Pro	Arg	Leu 35	Tyr	His	Gly	Cys	Tyr 40	Gly	Asp	Ile	Met	Thr 45	Met	Lys	
	tct Ser		-		_	-	_		_		_		_			490
_	ggt Gly 65		_	_		_		_	_	_		_				538
	cag Gln		_				-		_	-		-		_		586
	gtc Val															634
_	caa Gln	_			-								_	_	_	682
	gat Asp															730
	ctt Leu 145		_								_		_	_		778
_	aaa Lys				_		_	_								826
	tca Ser	_		_				_			_			_	_	874
	gac Asp															922
	aga Arg		_		tag	gca	aag (ctct	gtgg	gt g	ggcc	aggt	t gg	caga	gtge	976
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gaaat	gaata	tgca	Me	g at t Il 1	t gg e Gl	a aa y As	n As	c at n Me 5	g at t Il	t ac e Th	c tg r Cy	t at s Il 1	e As	t gga n Gly	410
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Cys L	aa ata ys Ile 30	a gca e Ala	gga Gly	gtt Val	aat Asn 35	ata Ile	aaa Lys	aca Thr	tta Leu	ctc Leu 40	aag Lys	cta Leu	tct Ser	gj aaa	506
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gta g Val A	ac tgo sp Cyr	aca Thr	gaa Glu	aaa Lys	agg Arg	gaa Glu	caa Gln 85	ttc Phe	tgc Cys	cca Pro	ccg Pro	cca Pro 90	cct Pro	cag Gln	650
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Glu L	aa gta ys Va] 10	gct Ala	gtt Val	ctc Leu	tgt Cys 115	aaa Lys	gaa Glu	aac Asn	tat Tyr	cta Leu 120	ctt Leu	cca Pro	gaa Glu	gca Ala	746
aaa ga Lys Gi 125	aa att lu Ile	gta Val	tgt Cys	aaa Lys 130	gat Asp	gga Gly	cga Arg	tgg Trp	caa Gln 135	tca Ser	tta Leu	cca Pro	cgc Arg	tgt Cys 140	794

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														gtt Val 235		1082
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ccg Pro	ctg Leu	ccc Pro	ttg Leu 290	ccg Pro	gcc Ala	ggc	aac Asn	tgc Cys 295	acg Thr	gac Asp	gag Glu	gag Glu	300 ggc	atc Ile	tgc Cys	1211
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aaa Lys	ctc Leu 480	tac Tyr	gac Asp	ctg Leu	cat His	ggt Gly 485	gac Asp	tgc Cys	agc Ser	tac Tyr	gtt Val 490	ctg Leu	t <i>cc</i> Ser	aag Lys	aaa Lys	1787
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		ctg Leu														2747
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		acc Thr 945														3179
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144

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Phe	Ser	Glu	Glu	Thr 145	Leu	aca Thr	Thr	Ala	Met 150	Thr	Ser	Thr	Pro	Pro 155	Ile	480
Thr	Ser	Ser	Ile 160	Thr	Pro	acc Thr	Asn	Thr 165	Val	Thr	Ser	Met	Thr 170	Thr	Met	528
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Ile	Leu 190	Ser	Ser	Thr	Pro	gtc Val 195	Pro	Ser	Thr	Glu	Arg 200	Thr	Thr	Ser	His	624
Thr 205	Thr	Asn	Ile	Asn	Pro 210	gta Val	Ser	Thr	Leu	Val 215	Thr	Thr	Leu	Pro	Thr 220	672
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Val 285	Thr	Thr	Thr	Thr	Lys 290	Thr	Thr	Ser	His	Ser 295	Thr	Thr	Ser	Phe	Thr 300	
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	gtt Val															1008
	tct Ser			_	_										-	1056
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	act Thr															1296
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	gtt Val															1536
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	gaa Glu 1070				Ser					Ala						3264
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Thr	agt Ser	Glu	Thr	Trp	Leu	Ser	Asn	Ser	Ser 1110	Val	Ile	Pro	Leu	Pro 1115	Leu	3360
Pro	ggc Gly	Val	Ser L120	Thr	Ile	Pro	Leu :	Thr L125	Met	ГÀВ	Pro	Ser	Ser 1130	Ser	Leu	3408
Pro		Ile 1135	Leu	Arg	Thr	Ser	Ser L140	Lys	Ser	Thr	His :	Pro 1145	Ser	Pro	Pro	3456
Thr	act Thr 1150	Arg	Thr	Ser	Glu I	Thr 1155	Pro	Val	Ala	Thr	Thr L160	Gln	Thr	Pro	Thr	3504
Thr 1165		Thr	Ser	Arg	Arg L170	Thr	Thr	Arg	Ile 1	Thr 175	Ser	Gln	Met	Thr	Thr L180	3552
Gln	tcc Ser	Thr	Leu I	Thr 1185	Thr	Thr	Ala	Gly 1	Thr 1190	Cys	Asp	Asn	Gly	Gly 1195	Thr	3600
Trp	gaa Glu	Gln	Gly L200	Gln	Сув	Ala	Cys	Leu 1205	Pro	Gly	Phe	Ser 1	Gly 1210	Asp	Arg	3648
Сув		Leu 1215	Gln	Thr	Arg	Cys 1	Gln 1220	Asn	Gly	Gly	Gln 1	Trp 1225	Asp	Gly	Leu	3696
ГÀЗ	tgc Cys 1230	Gln	Cys	Pro	Ser 1	Thr 1235	Phe	Tyr	Gly	Ser 1	Ser .240	Сув	Glu	Phe	Ala	3744
Val 1245	gaa Glu	Gln	Val	qaA I	Leu 250	qsA	Ala	Glu	Asp 1	Phe .255	Сув	Arg	His	Ala J	Gly 1260	3792
ctt	cac	CTT	caa	999	tgt	gga	gat	cct	gtc	cct	gag	gaa	tgg	cag	cat	3840

Leu His Leu Gln Gly Cys Gly Asp Pro Val Pro Glu Glu Trp Gln His cgt ggt gga cta cct ggt cct gct gga gat gcc ctt cag ccc cca gct 3888 Arg Gly Gly Leu Pro Gly Pro Ala Gly Asp Ala Leu Gln Pro Pro Ala gga gag cga gta tga gcaggtgaag accacgctga aggaggggct gcagaacgcc 3943 Gly Glu Arg Val 1295 agccaggatg tgaacagctg ccaggactcc cagaccctgt gttttaagcc tgactccatc 4003 aaggtgaaca acaacagcaa gacagagetg accccggcag ccatctgccg cgcgccgctc 4063 ccacgggcta tgaagagttc tacttcccct tggtggaggc cacccggctc cgctgtgtca 4123 ccaaatgcac gtctggggtg gacaacgcca tcgactgtca ccagggccag tgcgttctgg 4183 agacgagcgg teccaegtgt egetgetaet ecaeegaeae geaetggtte tetggeeege 4243 gctgcgaggt ggccgtccac tggagggcgc tggtcggggc ctgacggccg gcgcgctg 4303 ctggtgctgc tgctcgtggc gctgggcgtc cgggcggtgc gctccggatg gtggggcggc 4363 cagcgccgag gccggtcctg ggaccaggac aggaaatggt tcgagacctg ggatgaggaa 4423 gtcgtgggca ctttttcaaa ctggggtttc gaggacgacg gaacagacaa ggatacaaat 4483 ttctatgtgg ccttggagaa cgtgacacca ctatgaaggt gcacatcaag aqacccqaqa 4543 tgacctcgtc ctcagtgtga gcctgcgggg ccccttcacc acccctccg ccctgccccg 4603 gacacaaggg tetgcattge gtecatttea agaggtgace ceaggacgeg ggcageceag 4663 gctcctgctg ttcttgggca agatgagact gttcccccaa atcccatcct tctccttcca 4723 acttggctga aacccacctg gagacgcagt tcacgtccag gctcttccac tgtggaatct 4783 tgggcaagtc agtaacgagc ctcagtttcc tcacctgcaa aacgggtaca gcattcctgt 4843 atgatacgtc acgccgttgt tgtgaaaacc acatagactt ggtcaattct cggtcctact 4903 etgecetece gteteagece tegtgttgee attgeetete teggateete caateeteae 4963 gtccttcacc tggtctctgg ccctggttct tattttctct caattcccta ctgcctgttt 5023 5083 aactccctgc tgcatctctt gctcccattc cttagacgtc ctcccctttt gaccccgttc 5143 cttcatccat cetgcacccc agtcccccag ccctaaatcc tecetectet ceteacatce 5203 tggcccctag caaggtatag atagcctctg tgtcttagga taccccgggt gctgttccct 5263 eggteatect gttgeecagt teccegttte tettgetete attectgtat cettteecet 5323 tttgagcccg tccattcatc ggttctgccc ccgactcccc cagccctaaa taccccagct 5383 getgtteece ceateacet getgeceaat tetttattet ceaccettt eteteacee 5443

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ccagtcacct ctaccccagc tctccaggac acagcgctcc caactctgag tgacgtccca 180

cctctggtcc ttgcagcaca accaacgtgg gaatcacacc ctccagacct cccacagctc 240
caccccagac tgggcgccgg ccctgcctcc atttcagctg tgacaacctc agagccgtgt 300
tggcccaagc atg aca agg acg tat gaa aac ttc cag tac ttg gag aat 349
Met Thr Arg Thr Tyr Glu Asn Phe Gln Tyr Leu Glu Asn

aag gtg aaa gtc cag ggg ttt aaa aat ggg cca ctt cct ctc cag tcc 397
Lys Val Lys Val Gln Gly Phe Lys Asn Gly Pro Leu Pro Leu Gln Ser
15 20 25

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Leu Leu Gln Arg Leu Cys Ser Gly Pro Cys His Leu Leu Leu Ser Leu
30 35 40 45

ggc ctc ggc ctc ctg ctg gtc atc atc tgt gtg gtt gga ttc caa 493
Gly Leu Gly Leu Leu Leu Val Ile Ile Cys Val Val Gly Phe Gln
50 55 60

aat tcc aaa ttt cag agg gac ctg gtg acc ctg aga aca gat ttt agc
Asn Ser Lys Phe Gln Arg Asp Leu Val Thr Leu Arg Thr Asp Phe Ser
65 70 75

aac ttc acc tca aac act gtg gcg gag atc cag gca ctg act tcc cag
Asn Phe Thr Ser Asn Thr Val Ala Glu Ile Gln Ala Leu Thr Ser Gln
80
85

ggc agc agc ttg gaa gaa acg ata gca tct ctg aaa gct gag gtg gag 637 Gly Ser Ser Leu Glu Glu Thr Ile Ala Ser Leu Lys Ala Glu Val Glu 95 100 105

ggt Gly 110	Phe	Lys	cag Gln	gaa Glu	cgg Arg 115	Gln	gca Ala	Gly aaa	gta Val	tct Ser 120	gag Glu	ctc Leu	cag Gln	gaa Glu	cac His 125	685
	acg Thr															733
	gtc Val		-			-	_		_	_	_	_	_	_		781
	gac Asp															829
	gag Glu 175															877
	cac His															925
	gag Glu															973
	aac Asn					_			_	_						1021
	tac Tyr															1069
-	gat Asp 255	_		_						_			_			1117
	cca Pro															1165
	cac His															1213
	tac Tyr				-		_		_		_		_	-		1261
	cac His	tga	get	gcct	ttgg	gtggg	gac (cacco	egged	ca ca	agaaa	atggo	ggt ggt	-ggga	agga	1317
gga	ctctl	tet (cacga	acct	cc to	egcaa	agaco	gct	ctg	ggag	agaa	aataa	agc a	actg	ggagat	1377
tgg	aagca	act 9	gctaa	acati	tt to	gaatt	tttt	tet	cttt	aat	ttta	aaaa	aga t	ggta	atagtg	1437
ttc	ttaag	get (tttal	tttt	tt tt	ccaa	actt	t taa	aaagt	caa	ctto	catga	ag d	tata	atttt	1497

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1531

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gtcagatgtg ccacco	ccgcc acaactg	gcc aatggggtga	cggaaggcct ggact	atggc 180
ttc atg aag gaa Met Lys Glu 1	gta aca ttc (Val Thr Phe 1 5	cac tgt cat ga His Cys His Gl	u Gly Tyr Ile Lei	g cac 228 1 His 15
ggt gct cca aaa (Gly Ala Pro Lys 1	ctc acc tgt ca Leu Thr Cys G 20	ag tca gat ggc ln Ser Asp Gly 25	aac tgg gat gca Asn Trp Asp Ala 30	gag 276 Glu
att cct ctc tgt a Ile Pro Leu Cys I 35	aaa cca gtc aa Lys Pro Val Aa	ac tgt gga cct sn Cys Gly Pro 40	cct gaa gat ctt Pro Glu Asp Leu 45	gcc 324 Ala
cat ggt ttc cct a His Gly Phe Pro A 50	Asn Gly Phe Se	ec ttt att cat er Phe Ile His 55	ggg ggc cat ata Gly Gly His Ile 60	cag 372 Gln
tat cag tgc ttt o Tyr Gln Cys Phe I 65	cct ggt tat as Pro Gly Tyr Ly 70	ag ctc cat gga /s Leu His Gly	aat tca tca aga Asn Ser Ser Arg 75	agg 420 Arg
tgc ctc tcc aat o Cys Leu Ser Asn (80	ggc tcc tgg ag Gly Ser Trp Se 85	gt ggc agc tca er Gly Ser Ser 90	cct tcc tgc ctg Pro Ser Cys Leu	cct 468 Pro 95
tgc aga tgt tcc a Cys Arg Cys Ser i	aca cca gta at Thr Pro Val II 100	t gaa tat gga le Glu Tyr Gly 105	act gtc aat ggg Thr Val Asn Gly 110	aca 516 Thr
gat ttt gac tgt g Asp Phe Asp Cys (115	gga aag gca go Gly Lys Ala Al	cc cgg att cag la Arg Ile Gln 120	tgc ttc aaa ggc Cys Phe Lys Gly 125	ttc 564 Phe
aag ctc cta gga o Lys Leu Leu Gly I 130	ctt tct gaa at Leu Ser Glu II 13	le Thr Cys Glu	gcc gat ggc cag Ala Asp Gly Gln 140	tgg 612 Trp
agc tct ggg ttc o Ser Ser Gly Phe F 145	cac cac ttt ga His His Phe GJ 150	aa cac act tct lu His Thr Ser	tgt ggt tct ctt Cys Gly Ser Leu 155	cca 660 Pro

atg Met 160	ata Ile	cca Pro	aat Asn	gcg Ala	ttc Phe 165	atc Ile	agt Ser	gag Glu	acc Thr	agc Ser 170	tct Ser	tgg Trp	aag Lys	gaa Glu	aat Asn 175	708
	ata Ile															756
	ctg Leu															804
	gag Glu															852
	act Thr 225															900
ctg Leu 240	gaa Glu	ggt Gly	tat Tyr	acg Thr	atg Met 245	gat Asp	aca Thr	gat Asp	acc Thr	aga Arg 250	tca Ser	atc Ile	acc Thr	tgt Cys	cag Gln 255	948
	gat Asp															996
	cct Pro															1044
	agt Ser															1092
ttt Phe	gag Glu 305	gga Gly	gtt Val	aac Asn	ata Ile	tca Ser 310	gta Val	tgt Cys	cag Gln	ctt Leu	gat Asp 315	gga Gly	acc Thr	tgg Trp	gag Glu	1140
	cca Pro															1188
gaa Glu	agt Ser	cca Pro	gaa Glu	cat His 340	gga Gly	ttt Phe	gtg Val	gtt Val	ggc Gly 345	agt Ser	aaa Lys	tac Tyr	acc Thr	ttt Phe 350	gaa Glu	1236
agc Ser	aca Thr	att Ile	att Ile 355	tat Tyr	cag Gln	tgt Cys	gag Glu	cct Pro 360	ggc Gly	tat Tyr	gaa Glu	cta Leu	gag Glu 365	gjå aaa	aac Asn	1284
	gaa Glu															1332
ata Ile	tgc Cys 385	aaa Lys	gag Glu	acc Thr	agg Arg	tgt Cys 390	gaa Glu	act Thr	cca Pro	ctt Leu	gaa Glu 395	ttt Phe	ctc Leu	aat Asn	61 A 888	1380

aaa gct gac att gaa aac agg acg act gga ccc aac gtg gta tat tcc Lys Ala Asp Ile Glu Asn Arg Thr Thr Gly Pro Asn Val Val Tyr Ser 400 415	1428
tgc aac aga ggc tac agt ctt gaa ggg cca tct gag gca cac tgc aca Cys Asn Arg Gly Tyr Ser Leu Glu Gly Pro Ser Glu Ala His Cys Thr 420 425 430	1476
gaa aat gga acc tgg agc cac cca gtc cct ctc tgc aaa cca aat cca Glu Asn Gly Thr Trp Ser His Pro Val Pro Leu Cys Lys Pro Asn Pro 435 440 445	1524
tgc cct gtt cct ttt gtg att ccc gag aat gct ctg ctg tct gaa aag Cys Pro Val Pro Phe Val Ile Pro Glu Asn Ala Leu Leu Ser Glu Lys 450 455 460	1572
gag ttt tat gtt gat cag aat gtg tcc atc aaa tgt agg gaa ggt ttt Glu Phe Tyr Val Asp Gln Asn Val Ser Ile Lys Cys Arg Glu Gly Phe 465 470 475	1620
ctg ctg cag ggc cac ggc atc att acc tgc aac ccc gac gag acg tgg Leu Leu Gln Gly His Gly Ile Ile Thr Cys Asn Pro Asp Glu Thr Trp 480 485 490 495	1668
aca cag aca agc gcc aaa tgt gaa aaa atc tca tgt ggt cca cca gct Thr Gln Thr Ser Ala Lys Cys Glu Lys Ile Ser Cys Gly Pro Pro Ala 500 505 510	1716
cac gta gaa aat gca att gct cga ggc gta cat tat caa tat gga gac His Val Glu Asn Ala Ile Ala Arg Gly Val His Tyr Gln Tyr Gly Asp 515 520 525	1764
atg atc acc tac tca tgt tac agt gga tac atg ttg gag ggt ttc ctg Met Ile Thr Tyr Ser Cys Tyr Ser Gly Tyr Met Leu Glu Gly Phe Leu 530 535 540	1812
agg agt gtt tgt tta gaa aat gga aca tgg aca tca cct cct att tgc Arg Ser Val Cys Leu Glu Asn Gly Thr Trp Thr Ser Pro Pro Ile Cys 545 550 555	1860
aga gct gtc tgt cga ttt cca tgt cag aat ggg ggc atc tgc caa cgc Arg Ala Val Cys Arg Phe Pro Cys Gln Asn Gly Gly Ile Cys Gln Arg 560 575	1908
cca aat gct tgt tcc tgt cca gag ggc tgg gat ggg gcg cct ctg tga Pro Asn Ala Cys Ser Cys Pro Glu Gly Trp Asp Gly Ala Pro Leu 580 585 590	1956
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aagtccaaca tggtgctggg tcttgtttag taaacttgtt acttggggtt acttttttta	2316
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cggagt	tggg	cctga	atcco	ca ga	agcad	etggg	g ggt	-9999	gagg	aggt	gtta	act g	gtaaa	aatgca	24	4 (
agttgg	ataa	aagga	aggad	ec to	etego	ccaa	g g g(CCCC	Met				c Gli	g tct n Ser	2	95
act at Thr Il															34	43
att tt Ile Le		Arg													3	91
att go Ile Al 4															4:	3 9
aag to Lys Se 55	_				_	-							_	_	41	B 7
cgt tg Arg Cy															5:	35
agt gg Ser Gl															5	B3
gcc at Ala Me		Ala													6:	3 1
gga ac Gly Th	r Lev			His		Asn									6	79

aaa Lys 135	tct Ser	ggt Gly	tcc Ser	tat Tyr	gta Val 140	gct Ala	ctc Leu	act Thr	gtt Val	cag Gln 145	gga Gly	cgc Arg	cca Pro	cct Pro	150 Gly 999	727
tcg Ser	ccc Pro	cag Gln	att Ile	cca Pro 155	ctt Leu	gcc Ala	gac Asp	tct Ser	gaa Glu 160	gta Val	gag Glu	ccg Pro	tca Ser	gtc Val 165	att Ile	775
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tca Ser	acc Thr	cgt Arg 345	ata Ile	gca Ala	cct Pro	cat His	att Ile 350	att Ile	gga Gly	gca Ala	gaa Glu	gat Asp 355	gat Asp	gat Asp	ttt Phe	1351
ggt Gly	act Thr 360	gaa Glu	cat His	gaa Glu	cag Gln	atc Ile 365	aat Asn	gga Gly	cag Gln	tgc Cys	agc Ser 370	tgt Cys	ttc Phe	cag Gln	agc Ser	1399

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cat gta His Val		Ser													1495
tca gad Ser Asp	Leu 1														1543
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tct gtt Ser Val 440	Pro P														1639
ctc att Leu Ile 455															1687
aga gto Arg Val		Pro	_	_						_			_		1735
cgt agt Arg Ser	Met C		_		-	_	_	_		_				_	1783
gca gag Ala Glu		_	_	_	_	_		_		_				_	1831
gca gaa Ala Glu 520	Gln I		_	_				_	_	_	_		_	_	1879
gct gta Ala Val 535															1927
tat atc		His													1975
cac aaa His Lys	Arg (_		_	_	2023
aag aaa Lys Lys	_		_		_	_			_	_	_				2071
agc atc Ser Ile 600	Leu (2119
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Ile 615	Gly	Arg	Ala	Met	Glu 620	Leu	Gln	Lys	Ala	Arg 625	His	Pro	Lys	His	Leu 630	
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				tta Leu												2263
gcc Ala	aat Asn	tcc Ser 665	atg Met	tct Ser	tct Ser	gta Val	gct Ala 670	tca Ser	gjå aaa	gcc Ala	tct Ser	ttt Phe 675	tcc Ser	cag Gln	gaa Glu	2311
gga Gly	680 GJÀ āāā	aaa Lys	gag Glu	aat Asn	gat Asp	aca Thr 685	gga Gly	tca Ser	aag Lys	caa Gln	gtt Val 690	gga Gly	gaa Glu	aca Thr	tca Ser	2359
				acc Thr												2407
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				gtg Val												2503
	_	_	_	gct Ala			_	_		_		_	_			2551
				gag Glu		_					-	_		-	_	2599
				ctg Leu												2647
				ttg Leu 795												2695
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				tct Ser												2887

855					860					865					870	
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											atc Ile					2983
											gat Asp					3031
		_	_	_			_	_	_		att Ile 930				_	3079
											aat Asn					3127
											aaa Lys					3175
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Leu					Tyr					Glu	ctc Leu 1010					3319
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			Lys					Tyr			ctg Leu		Glu			3415
		Leu					Asp				gtt Val	Leu				3463
_	Lys		_	_		Thr	_	_	_		cac His	_		_		3511
Val		_	_	_	Thr		_	_	_	Gln	1030 GJA aaa	_		_		3559
	-			Val			_		Asp		ggc Gly	_	_	Ile		3607

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cca tta cca cag tca aca cct ggc gaa gga gat aat gat gaa gaa gat Pro Leu Pro Gln Ser Thr Pro Gly Glu Gly Asp Asn Asp Glu Glu Asp 1145 1150 1155	3751
cct tca aaa tta aaa gag gag cag cat ggc att tca gtc act ggt ttg Pro Ser Lys Leu Lys Glu Glu Gln His Gly Ile Ser Val Thr Gly Leu 1160 1165 1170	3799
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gat ctg ttt gtg gct gag aga cag ttt gca aag gaa caa cat aca gat Asp Leu Phe Val Ala Glu Arg Gln Phe Ala Lys Glu Gln His Thr Asp 1210 1220	3943
ggg aca cta aag gaa gtt gga gaa gat tat caa atc gca atc cca gat Gly Thr Leu Lys Glu Val Gly Glu Asp Tyr Gln Ile Ala Ile Pro Asp 1225 1230 1235	3991
tca cac ctg cct gtc tca gaa gaa cgg tgg gca ttg gat gca cta aga Ser His Leu Pro Val Ser Glu Glu Arg Trp Ala Leu Asp Ala Leu Arg 1240 1245 1250	4039
aat ttg ggt ttg ttg aag cag ttg ctg gtg caa cag cta ggt ttg act Asn Leu Gly Leu Leu Lys Gln Leu Leu Val Gln Gln Leu Gly Leu Thr 1255 1260 1265 1270	4087
gag aag agc gtt cag gaa gac tgg caa cat ttc cca aga tac aga aca Glu Lys Ser Val Gln Glu Asp Trp Gln His Phe Pro Arg Tyr Arg Thr 1285 1280	4135
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gat gcc cgt gaa gca cat agt gat gag aat cca tca gaa ggt gat gga Asp Ala Arg Glu Ala His Ser Asp Glu Asn Pro Ser Glu Gly Asp Gly 1385 1390 1395	4471
gca gtt aac aag gaa gag aag gat gtt aat tta cgc atc tca gga aac Ala Val Asn Lys Glu Glu Lys Asp Val Asn Leu Arg Ile Ser Gly Asn 1400 1405 1410	4519
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gag gag gtt gct tcc tca ctt acc ctg cag ccc atg aca ggc atc cct Glu Glu Val Ala Ser Ser Leu Thr Leu Gln Pro Met Thr Gly Ile Pro 1435 1440 1445	4615
gct gtg gaa tcc acc cac cag cag caa cat tct cct cag aat act cac Ala Val Glu Ser Thr His Gln Gln Gln His Ser Pro Gln Asn Thr His 1450 1455 1460	4663
tcc gat ggg gca att tca cca ttc acc ccc gaa ttt ctg gtc cag cag Ser Asp Gly Ala Ile Ser Pro Phe Thr Pro Glu Phe Leu Val Gln Gln 1465 1470 1475	4711
cgc tgg gga gct atg gag tat tcc tgt ttt gag atc cag agt ccc tcc Arg Trp Gly Ala Met Glu Tyr Ser Cys Phe Glu Ile Gln Ser Pro Ser 1480 1485 1490	4759
tct tgt gca gat tca cag agc cag atc atg gag tac att cat aag ata Ser Cys Ala Asp Ser Gln Ser Gln Ile Met Glu Tyr Ile His Lys Ile 1495 1500 1505 1510	4807
gag gct gac ctt gaa cac tta aag aag gtg gag gaa agt tac acc att Glu Ala Asp Leu Glu His Leu Lys Lys Val Glu Glu Ser Tyr Thr Ile 1515 1520 1525	4855
ctt tgc caa agg ctg gct gga tca gcc ctc aca gac aag cac tca gat Leu Cys Gln Arg Leu Ala Gly Ser Ala Leu Thr Asp Lys His Ser Asp 1530 1535 1540	4903
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<210> 41

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cta Leu	cta Leu 70	gcc Ala	tat Tyr	gtg Val	aaa Lys	cac His 75	ctg Leu	aaa Lys	ggc ggc	cag Gln	aat Asn 80	gag Glu	gaa Glu	gcc Ala	ctg Leu	353
	agc Ser															401
	gca Ala															449
	tac Tyr															497
	gag Glu															545
	tgt Cys 150															593
	gga Gly															641
	gly aaa															689
	tat Tyr															737
	tct Ser															785
gta Val	tat Tyr 230	att Ile	agg Arg	gtt Val	ctc Leu	ctt Leu 235	gcc Ala	ctg Leu	aag Lys	ctt Leu	cag Gln 240	gat Asp	gaa Glu	gga Gly	cag Gln	833
	gct Ala															881
	cag Gln															929

ggg tct gtg Gly Ser Val				u Leu							977
aca ccc act Thr Pro Thr 295											1025
gca caa atg Ala Gln Met 310	atc caa Ile Gln	atc aag Ile Lys 315	gaa gc Glu Al	t aca a Thr	aac Asn	tgg Trp 320	cag Gln	cct Pro	aga Arg	GJÅ aaa	1073
caa gat agg Gln Asp Arg 325											1121
ttt gaa aag Phe Glu Lys							_	_		~	1169
gac ctg gct Asp Leu Ala	-	_	-	e Gly			_	_	_	-	1217
gaa cat ttt Glu His Phe 375											1265
aag caa gag Lys Gln Glu 390				_			_				1313
aaa tct caa Lys Ser Gln 405											1361
gaa aaa atg Glu Lys Met			_				_				1409
ttg gct aaa Leu Ala Lys				n Val							1457
agc ctc ctt Ser Leu Leu 455											1505
ttg ctg tgc Leu Leu Cys 470					Ala						1553
ata ttt taa Ile Phe 485	catagag	gtcacca	tta tcc	atttaa	at gg	gtett	cataa	a cta	aaata	agaa	1609
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<211> 1671

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Glu 65	Glu	Phe	Ile	Trp	Leu 70	His	Asp	Ala	Tyr	Val 75	Glu	Asn	Glu	Glu	Tyr 80	
						cca Pro										704
						aaa Lys										752
						atg Met										800
						gtt Val 135										848
						ctg Leu										896
						ctg Leu										944
						agg Arg										992
						gj aaa										1040
						ttg Leu 215										1088
						gtc Val										1136
						gct Ala										1184
						agc Ser										1232
						ggc										1280
ctg Leu	tca Ser 290	gac Asp	atg Met	ctg Leu	agg Arg	tac Tyr 295	tac Tyr	atg Met	cgt Arg	gac Asp	tca Ser 300	cag Gln	gca Ala	gcc Ala	aag Lys	1328
gac A sp	ctg Leu	ctg Leu	tac Tyr	cgg Arg	cgg Arg	ctg Leu	cgg Arg	gca Ala	ctg Leu	gcc Ala	gac Asp	tac Tyr	gag Glu	aat Asn	gcc Ala	1376

305	310		315	320
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Ala Glu Ser			cgc ttc gag cgc Arg Phe Glu Arg 350	
			aag tcc cgc cgg Lys Ser Arg Arg 365	
		e Glu Leu Ala	gag ctg gag ctc Glu Leu Glu Leu 380	
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<210> 43

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cgg Arg	gag Glu	ctc Leu	ttc Phe	cca Pro 85	aca Thr	tgg Trp	ctg Leu	ttg Leu	gtc Val 90	atg Met	gag Glu	atc Ile	ctc Leu	aat Asn 95	gtc Val	465
acg Thr	ctg Leu	gtg Val	ccc Pro 100	tac Tyr	gga Gly	aac Asn	gca Ala	cag Gln 105	gaa Glu	caa Gln	aat Asn	gtc Val	agt Ser 110	ggc Gly	agg Arg	513
tgg Trp	gag Glu	ttc Phe 115	aag Lys	tgc Cys	cag Gln	cat His	gga Gly 120	gaa Glu	gag Glu	gag Glu	tgc Cys	aaa Lys 125	ttc Phe	aac Asn	aag Lys	561
gtg Val	gag Glu 130	gcc Ala	tgc Cys	gtg Val	ttg Leu	gat Asp 135	gaa Glu	ctt Leu	gac Asp	atg Met	gag Glu 140	cta Leu	gcc Ala	ttc Phe	ctg Leu	609
acc Thr 145	att Ile	gtc Val	tgc Cys	atg Met	gaa Glu 150	gag Glu	ttt Phe	gag Glu	gac Asp	atg Met 155	gag Glu	aga Arg	agt Ser	ctg Leu	cca Pro 160	657
cta Leu	tgc Cys	ctg Leu	cag Gln	ctc Leu 165	tac Tyr	gcc Ala	cca Pro	gjà aaa	ctg Leu 170	tcg Ser	cca Pro	gac Asp	act Thr	atc Ile 175	atg Met	705
gag Glu	tgt Cys	gca Ala	atg Met 180	GJA aaa	gac Asp	cgc Arg	gly ggc	atg Met 185	cag Gln	ctc Leu	atg Met	cac His	gcc Ala 190	aac Asn	gcc Ala	753
cag Gln	cgg Arg	aca Thr 195	gat Asp	gct Ala	ctc Leu	cag Gln	cca Pro 200	cca Pro	cac His	gag Glu	tat Tyr	gtg Val 205	ccc Pro	tgg Trp	gtc Val	801
acc Thr	gtc Val 210	aat Asn	gjå aaa	aaa Lys	ccc Pro	ctt Leu 215	gga Gly	aga Arg	tca Ser	gac Asp	cca Pro 220	gct Ala	cct Pro	tac Tyr	cct Pro	849
tgt Cys 225	ctg Leu	cca Pro	gtt Val	gta Val	cca Pro 230	Gly aaa	caa Gln	gaa Glu	gcc Ala	gga Gly 235	tgt Cys	ctg Leu	ccc Pro	ttc Phe	ctc Leu 240	897
aac Asn	cag Gln	ctc Leu	cct Pro	cag Gln 245	gag Glu	tgt Cys	ttg Leu	ctt Leu	caa Gln 250	gtg Val	atg Met	gcc Ala	ggt Gly	gag Glu 255	ctg Leu	945
cgg Arg	aga Arg	gct Ala	cat His 260	gga Gly	agg Arg	cga Arg	gtg Val	gga Gly 265	acc Thr	cgg Arg	ctg Leu	cct Pro	gcc Ala 270	ttt Phe	ttt Phe	993
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ggc Gly	agg Arg 210	aga Arg	cct Pro	țcc Ser	tcg Ser	ccc Pro 215	agt Ser	tcg Ser	cat His	gjà aaa	cag Gln 220	Met	cta Leu	acc Thr	cca Pro	672
aag Lys 225	atc Ile	aac Asn	aag Lys	ttg Leu	gag Glu 230	Lys	gct Ala	gtt Val	gct Ala	gca Ala 235	gca Ala	cac His	acc Thr	ttc Phe	ttc Phe 240	720
gtg Val	Gly	aat Asn	cct Pro	gag Glu 245	cac His	atg Met	gaa Glu	atg Met	cag Gln 250	cag Gln	aac Asn	cta Leu	gac Asp	tat Tyr 255	tac Tyr	768
caa Gln	acc Thr	atg Met	tct Ser 260	gga Gly	gtg Val	aag Lys	gag Glu	gcc Ala 265	gac Asp	ttc Phe	aag Lys	gat Asp	ctt Leu 270	gag Glu	act Thr	816
caa Gln	ccc Pro	cat His 275	atg Met	caa Gln	gaa Glu	ttt Phe	cga Arg 280	ctg Leu	gga Gly	gtg Val	cga Arg	ctc Leu 285	tac Tyr	tca Ser	gag Glu	864
gaa Glu	cag Gln 290	cca Pro	cag Gln	gaa Glu	gct Ala	gtg Val 295	ccc Pro	cac His	cta Leu	gag Glu	gcg Ala 300	gcg Ala	ctg Leu	caa Gln	gaa Glu	912
tac Tyr 305	ttt Phe	gtg Val	gcc Ala	tat Tyr	gag Glu 310	gag Glu	tgc Cys	cgt Arg	gcc Ala	ctc Leu 315	tgc Cys	gaa Glu	Gl ^A aaa	ccc Pro	tat Tyr 320	960
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gcc Ala	atc Ile	aca Thr	gat Asp 340	cat His	tac Tyr	atc Ile	cag Gln	gtc Val 345	ctc Leu	aac Asn	tgt Cys	aag Lys	cag Gln 350	aac Asn	tgt Cys	1056
gtc Val	acg Thr	gag Glu 355	ctt Leu	gct Ala	tcc Ser	cac His	cca Pro 360	agt Ser	cga Arg	gag Glu	aag Lys	ccc Pro 365	ttt Phe	gaa Glu	gac Asp	1104
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385 999	aat Asn	tat Tyr	aca Thr	cag Gln	gct Ala 390	gtt Val	gaa Glu	tgt Cys	gcc Ala	aag Lys 395	acc Thr	tat Tyr	ctt Leu	ctc Leu	ttc Phe 400	1200
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atg Met	ctt Leu	gga Gly	gaa Glu 420	gaa Glu	cac His	acc Thr	aga Arg	tcc Ser 425	atc Ile	ggc Gly	ccc Pro	cgt Arg	gag Glu 430	agt Ser	gcc Ala	1296
aag Lys	gag Glu	tac Tyr 435	cga Arg	cag Gln	cga Arg	agc Ser	cta Leu 440	ctg Leu	gaa Glu	aaa Lys	gaa Glu	ctg Leu 445	ctt Leu	ttc Phe	ttc Phe	1344
gct	tat	gat	gtt	ttt	gga	att	ccc	ttt	gtg	gat	ccg	gat	tca	tgg	act	1392

Ala	Tyr 450	Asp	Val	Phe	Gly	Ile 455	Pro	Phe	Val	Asp	Pro 460	Asp	Ser	Trp	Thr	
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	gaa Glu		_	-	_			_						_	_	1488
	atc Ile															1536
_	aga Arg	_			_							-			_	1584
	acc Thr 530	_					_				_				_	1632
_	ggc Gly	-			_			_	_		_	_	_	_		1680
	gtg Val	_	_				_					-				1728
	act Thr															1776
	ctg Leu															1824
	aac Asn 610		_		_			_		-					_	1872
	gat Asp															1920
gcc Ala	atc Ile	gaa Glu	gag Glu	gtc Val 645	cag Gln	gca Ala	gag Glu	agg Arg	aag Lys 650	gat Asp	gat Asp	agt Ser	cat His	cca Pro 655	gtc Val	1968
	gtg Val															2016
	ccc Pro															2064
	gly ggg	_		_								_	_	_	_	2112

	690					695					700					
aag Lys 705	acc Thr	gtg Val	acg Thr	gca Ala	gag Glu 710	gtg Val	cag Gln	cct Pro	cag Gln	tgt Cys 715	gga Gly	aga Arg	gcc Ala	gtg Val	gga Gly 720	2160
ttc Phe	tct Ser	tca Ser	ggc ggc	act Thr 725	gaa Glu	aac Asn	cca Pro	cat His	gga Gly 730	gtg Val	aag Lys	gct Ala	gtc Val	acc Thr 735	agg Arg	2208
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														ctc Leu		2304
														gcc Ala		2352
														gaa Glu		2400
		aag Lys				tga	ca ç	gegt	ccago	gt ca	agac	gato	g ggt	gact	aga	2453
ccc	atgga	aga g	ggaa	eteti	c to	gcact	cctga	a gct	ggc	cagc	acat	cggg	ggc t	gcag	gagcag	2513
tga	geeta	aca t	tctg	ccact	cc ag	gccga	3ggg	g aco	cctgo	ctca	cago	cctt	cta d	catgo	gtgcta	2573
ctg	ctctt	gg a	agtg	gacat	g ac	ccaga	acaco	gca	ccc	cctg	gato	tgg	ctg a	aggg	ctcagg	2633
aca	caggo	ecc a	agcca	accc	cc ag	3999¢	cctco	c aca	aggco	gct	gcat	aaca	agc g	gatad	cagtac	2693
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<220>

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ccagccacgt ctccttggct gtggggatga tctgggaggc tggcagcagg aagccatagc 180
gcccagtgtc ccggagctcg aaggtgaagg agtacttgat gccctggctg taggtccagt 240

caatagtget tecaetgget tgataaattg cettgatgat getgeeatag ttgaaettgg	300
tecegtagag agaggeeagg getgteaeag eageettgga aagetgatee ageteateet	360
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agcctgctgt gtgggaccga gtcttgcgcc ac atg cga ttc gtg ctg tgc gtg Met Arg Phe Val Leu Cys Val 1 5	653
aag gca aag cca tca ggg ttg gtg acg atc tcc agg aag atc act caa Lys Ala Lys Pro Ser Gly Leu Val Thr Ile Ser Arg Lys Ile Thr Gln 10 15 20	701
gac tac ggg cag gat gca gct ttc acc gcc att ctc gac acc ttg gac Asp Tyr Gly Gln Asp Ala Ala Phe Thr Ala Ile Leu Asp Thr Leu Asp 25 30 35	749
atc ttc ctg gag atc gtc acc aac cct gat ggc ttt gcc ttc acg cac Ile Phe Leu Glu Ile Val Thr Asn Pro Asp Gly Phe Ala Phe Thr His 40 45 50 55	797
age acg aat ege atg tgg ege aag act egg tee eac aca gea gge tee Ser Thr Asn Arg Met Trp Arg Lys Thr Arg Ser His Thr Ala Gly Ser 60 65 70	845
ctc tgt att ggc gtg gac ccc aac agg aac tgg gac gct ggc ttt ggg Leu Cys Ile Gly Val Asp Pro Asn Arg Asn Trp Asp Ala Gly Phe Gly 75 80 85	893
ttg tcc gga gcc agc agt aac ccc tgc tcg gag act tac cac ggc aag Leu Ser Gly Ala Ser Ser Asn Pro Cys Ser Glu Thr Tyr His Gly Lys 90 95 100	941
ttt gcc aat tcc gaa gtg gag gtc aag tcc att gta gac ttt gtg aag Phe Ala Asn Ser Glu Val Glu Val Lys Ser Ile Val Asp Phe Val Lys 105 110 115	989
gac cat ggg aac atc aag gcc ttc atc tcc atc cac agc tac tcc cag Asp His Gly Asn Ile Lys Ala Phe Ile Ser Ile His Ser Tyr Ser Gln 120 125 130 135	1037
ctc ctc atg tat ccc tat ggc tac aaa aca gaa cca gtc cct gac cag Leu Leu Met Tyr Pro Tyr Gly Tyr Lys Thr Glu Pro Val Pro Asp Gln 140 145 150	1085
gat gag ctg gat cag ctt tcc aag gct gct gtg aca gcc ctg gcc tct Asp Glu Leu Asp Gln Leu Ser Lys Ala Ala Val Thr Ala Leu Ala Ser 155 160 165	1133
ctc tac ggg acc aag ttc aac tat ggc agc atc atc aag gca att tat Leu Tyr Gly Thr Lys Phe Asn Tyr Gly Ser Ile Ile Lys Ala Ile Tyr 170 175 180	1181
caa gcc agt gga agc act att gac tgg acc tac agc cag ggc atc aag	1229

18		GIY	ser	Thr	190		Trp	Tnr	Tyr	Ser 195	Gln	GIÀ	Ile	Lys	
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ctg cc Leu Pr	a gcc o Ala	tcc Ser	cag Gln 220	atc Ile	atc Ile	ccc Pro	aca Thr	gcc Ala 225	aag Lys	gag Glu	acg Thr	tgg Trp	ctg Leu 230	Ala	1325
ctt cte	g acc ı Thr	atc Ile 235	atg Met	gag Glu	cac His	acc Thr	ctg Leu 240	Asn	cac His	ccc Pro	tac Tyr	tga	gct	gacc	1374
ctttga	cacc	cttc	ttgt	cc t	ecte	tctg	g cc	ccat	ccag	gca	acca	aat	aaag	tttgag	1434
tgtacc	agga	acag	aatc	ct g	gggc	ttgc	a aa	aaaa	aaaa	aa					1476
<: <: <: <: <:	210> 211> 212> 213> 220> 221> 222>	1769 DNA Homo CDS (137))					•					
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gccgtc	gccc	aggat	tggg	ct g	ggaat	gaag	g cga	atgta	agcc	ttt	taaga	aga 1	tttg	ctctga	120
cccatc	gaa	gteca	at	Met				r Āsī						a aat s Asn O	169
pro Phe	tat Tyr	ctg Leu 15	gct Ala	ctg Leu	caa Gln	aag Lys	tgc Cys 20	cgc Arg	cct Pro	gac Asp	ttg Leu	tgc Cys 25	agc Ser	aaa Lys	217
gtg gcc Val Ala	caa Gln 30	atc Ile	cat His	ggc Gly	att Ile	gtc Val 35	tta Leu	gta Val	ccc Pro	tgc Cys	aaa Lys 40	gga Gly	agc Ser	ctg Leu	265
tcg ago Ser Ser 45	Ser	atc Ile	cag Gln	tct Ser	act Thr 50	tgt Cys	cag Gln	ttt Phe	gag Glu	tcc Ser 55	tac Tyr	att Ile	ttg Leu	ata Ile	313
cct gtg Pro Val	gaa . Glu	gag Glu	cat His	ttt Phe 65	cag Gln	acc Thr	tta Leu	aat Asn	gga Gly 70	aag Lys	gat Asp	gtc Val	ttt Phe	att Ile 75	361
caa ggg	aac Asn	agg Arg	att Ile 80	aaa Lys	tta Leu	gga Gly	gct Ala	ggt Gly 85	ttt Phe	gcc Ala	tgt Cys	ctt Leu	ctc Leu 90	tca Ser	409
gtg ccc	att	ctc	ttt	gaa	gaa	act	ttc	tac	aat	gaa	aaa	gaa	gag	agt	457

Val	Pro	Ile	Leu 95	Phe	Glu	Glu	Thr	Phe 100	Tyr	Asn	Glu	Lys	Glu 105	Glu	Ser	
	_		_	_		_			_	_	_	-	gag Glu	_		505
													acc Thr			553
_	_	_			_		_				_		gac Asp			601
	_				_			_	_	_		_	aag Lys	-		649
-				_									tgc Cys 185		_	697
_		_		_			_		_		_	_	cag Gln			745
													cat His			793
			_								_		gca Ala	-		841
					222											889
_		_	ttt Phe					_	_			_	Leu	_	_	003
Asp	Ala	Ala	Phe ggt	Asn 240 gtg	Lys aaa	Ile ccg	Thr	Arg	Ser 245 agc	Leu ttt	Gln aac	Asp		Gln 250 cgt	Gln	937
Asp aaa Lys aaa	Ala gat Asp	Ala att Ile	ggt Gly 255 ctg	Asn 240 gtg Val gct	Lys aaa Lys cag	ccg Pro	Thr gag Glu aac	ttc Phe 260	Ser 245 agc Ser	Leu ttt Phe acc	Gln aac Asn tcc	Asp ata Ile	Leu cct Pro	Gln 250 cgt Arg	Gln gcc Ala	
Asp aaa Lys aaa Lys	Ala gat Asp aga Arg	Ala att Ile gag Glu 270 tgc	ggt Gly 255 ctg Leu	Asn 240 gtg Val gct Ala	Lys aaa Lys cag Gln aaa	ccg Pro ctg Leu	Thr gag Glu aac Asn 275	ttc Phe 260 aaa Lys	Ser 245 agc Ser tgc Cys	ttt Phe acc Thr	Gln aac Asn tcc Ser	Asp ata Ile cca Pro 280 cag	cct Pro 265	Gln 250 cgt Arg cag Gln	Gln gcc Ala aag Lys	937
Asp aaa Lys Lys ctt Leu cag	gat Asp aga Arg gtc Val 285	Ala att Ile gag Glu 270 tgc Cys	ggt Gly 255 ctg Leu ttg Leu	Asn 240 gtg Val gct Ala cga Arg	Lys aaa Lys Cag Gln aaa Lys	ccg Pro ctg Leu gtg Val 290	gag Glu aac Asn 275 gtg Val	ttc Phe 260 aaa Lys cag Gln	ser 245 agc ser tgc Cys ctc Leu	ttt Phe acc Thr att Ile	aac Asn tcc Ser aca Thr 295	Asp ata Ile cca Pro 280 cag Gln	cct Pro 265 cag Gln	Gln 250 cgt Arg cag Gln cca Pro	gcc Ala aag Lys agc Ser	937 985
aaa Lys aaa Lys ctt Leu cag Gln 300	gat Asp aga Arg gtc Val 285 aga Arg	Ala att Ile gag Glu 270 tgc Cys gtg Val	ggt Gly 255 ctg Leu ttg Leu aac Asn	Asn 240 gtg Val gct Ala cga Arg ctg Leu	Lys aaa Lys cag Gln aaa Lys gag Glu 305 gtg	Ccg Pro ctg Leu gtg Val 290 acc Thr	gag Glu aac Asn 275 gtg Val atg Met	ttc Phe 260 aaa Lys cag Gln tgt Cys	ser 245 agc ser tgc Cys ctc Leu gct Ala	ttt Phe acc Thr att Ile gat Asp 310	aac Asn tcc Ser aca Thr 295 gat Asp	Asp ata Ile cca Pro 280 cag Gln ctg Leu tgg	cct Pro 265 cag Gln tct Ser	Gln 250 cgt Arg cag Gln cca Pro tca Ser	gcc Ala aag Lys agc Ser gtc Val 315	937 985 1033

	335	340		345	
			gct gcc att ga Ala Ala Ile Gl 36	lu Tyr Ile Arg	1225
caa gga agc Gln Gly Ser 365	ctc tct gct Leu Ser Ala	aaa ccc cct Lys Pro Pro 370	gag tot gag gg Glu Ser Glu Gl 375	ga ttt gga gac ly Phe Gly Asp	1273
agg ctg ttc Arg Leu Phe 380	ctt aag cag Leu Lys Gln 385	aga atg agc Arg Met Ser	tta ctc tct ca Leu Leu Ser Gl 390	ag atg act tcg In Met Thr Ser 395	1321
tct ccc acc Ser Pro Thr	gac tgc ctg Asp Cys Leu 400	ttt aag cac Phe Lys His	att gca tca gg Ile Ala Ser Gl 405	gt aac cag aaa Ly Asn Gln Lys 410	1369
gaa gtg gag Glu Val Glu	aga ctt ctg Arg Leu Leu 415	agc caa gag Ser Gln Glu 420	gac cat gat as Asp His Asp Ly	aa gat acc gtc /s Asp Thr Val 425	1417
caa aag atg Gln Lys Met 430	tgt cac cct Cys His Pro	ctc tgc ttc Leu Cys Phe 435	tgc gat gac tg Cys Asp Asp Cy 44	s Glu Lys Leu	1465
gtc tct ggg Val Ser Gly 445	agg ttg aat Arg Leu Asn	gat ccc tca Asp Pro Ser 450	gtt gtc act co Val Val Thr Pr 455	a ttc tcc aga o Phe Ser Arg	1513
gac gac agg Asp Asp Arg 460	ggg cac acc Gly His Thr 465	cct ctc cat Pro Leu His	gtg gct gct gt Val Ala Ala Va 470	c tgt ggg cag al Cys Gly Gln 475	1561
gca tcc ctc Ala Ser Leu	atc gac ctc Ile Asp Leu 480	ctg gtt tcc Leu Val Ser	aag ggc gcc at Lys Gly Ala Me 485	g gta aat gcc t Val Asn Ala 490	1609
			cac ctg gcc tg His Leu Ala Cy		1657
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gtg cag gac Val Gln Asp 525	aac aat ggg Asn Asn Gly	aat acg cca Asn Thr Pro 530	cat gta ttg cg His Val Leu Ar 535	g ccg ctc tag g Pro Leu	1753
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<213> Homo sapiens

<220>

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Glı	ı Ala	Thr	Ala	Pro 125	Pro	Ser	Ile	Phe	Leu 130	Pro	Phe	Pro	Phe	Gln 135	Pro		
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gco	ctc Leu	cca Pro 155	cca Pro	ctg Leu	ctg Leu	cgg Arg	cgc Arg 160	ggc Gly	cgg Arg	ccc Pro	cgg Arg	ccg Pro 165	tgt Cys	gct Ala	gcg Ala	1	252
cti Lei	gcc Ala 170	tta Leu	cca Pro	gct Ala	ctc Leu	tcc Ser 175	tcg Ser	ctt Leu	ttc Phe	tct Ser	ccc Pro 180	gtt Val	ttc Phe	tct Ser	ctg Leu	1	300
ctt Let 185	tct Ser	ctc Leu	caa Gln	ctg Leu	cca Pro 190	gcc Ala	gat Asp	cgg Arg	gtc Val	agg Arg 195	caa Gln	gtc Val	cat His	ccc Pro	gtc Val 200	1	348
ct <u>c</u> Lei	aga Arg	gcc Ala	cca Pro	ggc Gly 205	ccc Pro	cct Pro	tcg Ser	acc Thr	tct Ser 210	aaa Lys	cag Gln	atc Ile	cct Pro	cct Pro 215	ctt Leu	1	396
Cto	gga Gly	gac Asp	ctc Leu 220	cct Pro	ttc Phe	caa Gln	gcc Ala	tgc Cys 225	ctg Leu	gac Asp	ggc	tgt Cys	tct Ser 230	gtg Val	act Thr	1	444
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														att Ile		384
		_		_		_		_		_	_		_	ttg Leu 60		432
		-						_		_		_	_	gga Gly		480
_		-		_	_			_				_		aaa Lys	_	528
	cag Gln 95	_		_		_			_	-		taa	gcaa	attaa	iaa	577
aaat	tttg	gtt a	agcad	ctcci	t ca	agtga	attgt	: tt	tcad	cctt	tati	tgt	gtt a	attci	tttag	637
tct	cgaca	aca a	ataca	agaag	ga to	3										659

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<400> 49

<213> Homo sapiens

<220>
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<222> (187)..(1188)

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60

372

ggaattcccg ggtcgacgat ttcgtgcgac ggctgctgtg tctcctggaa agggattccc

Trp Arg Arg Ala Val Trp Glu Lys Asn Met Lys Met Ile Glu Leu His
50 55 60

aat ggg gaa tac agc caa ggg aaa cac agc ttc aca atg gcc atg aat 42

tgg agg aga gca gtg tgg gaa aag aat atg aaa atg att gaa ctg cac

aat ggg gaa tac agc caa ggg aaa cac agc ttc aca atg gcc atg aat 420 Asn Gly Glu Tyr Ser Gln Gly Lys His Ser Phe Thr Met Ala Met Asn 65 70 75

gcc Ala	ttt Phe 80	gga Gly	gac Asp	atg Met	acc Thr	aat Asn 85	gaa Glu	gaa Glu	ttc Phe	agg Arg	cag Gln 90	gtg Val	atg Met	aat Asn	ggt Gly	468
ttt Phe 95	caa Gln	tac Tyr	cag Gln	aag Lys	cac His 100	agg Arg	aag Lys	ej aaa	aaa Lys	cag Gln 105	ttc Phe	cag Gln	gaa Glu	cgc Arg	ctg Leu 110	516
ctt Leu	ctt Leu	gag Glu	atc Ile	ccc Pro 115	aca Thr	tct Ser	gtg Val	gac Asp	tgg Trp 120	aga Arg	gag Glu	aaa Lys	ggc	tac Tyr 125	atg Met	564
act Thr	cct Pro	gtg Val	aag Lys 130	gat Asp	cag Gln	ggt Gly	cag Gln	tgt Cys 135	ggc Gly	tct Ser	tgt Cys	tgg Trp	gct Ala 140	ttt Phe	agt Ser	612
		ggt Gly 145														660
atc Ile	tca Ser 160	ctg Leu	aat Asn	gag Glu	cag Gln	aat Asn 165	ctg Leu	gta Val	gac Asp	tgc Cys	tct Ser 170	GJ À aaa	cct Pro	caa Gln	ggc	708
		ggc ggc						_	_						_	756
cag Gln	gag Glu	aac Asn	gga Gly	ggc Gly 195	ctg Leu	gac Asp	tct Ser	gag Glu	gaa Glu 200	tcc Ser	tat Tyr	cca Pro	tat Tyr	gag Glu 205	gca Ala	804
		gaa Glu														852
acc Thr	ggc	ttt Phe 225	gtg Val	gac Asp	atc Ile	cct Pro	aag Lys 230	cag Gln	gag Glu	aag Lys	gcc Ala	ctg Leu 235	atg Met	aag Lys	gca Ala	900
gtt Val	gca Ala 240	act Thr	gtg Val	ej Gaa	ccc Pro	att Ile 245	tct Ser	gtt Val	gct Ala	att Ile	gat Asp 250	gca Ala	ggt Gly	cat His	gag Glu	948
tcc Ser 255	ttc Phe	ctg Leu	ttc Phe	tat Tyr	aaa Lys 260	gaa Glu	ggc ggc	att Ile	tat Tyr	ttt Phe 265	gag Glu	cca Pro	gac Asp	tgt Cys	agc Ser 270	996
agt Ser	gaa Glu	gac Asp	atg Met	gat Asp 275	cat His	ggt Gly	gtg Val	ctg Leu	gtg Val 280	gtt Val	ggc Gly	tac Tyr	gga Gly	ttt Phe 285	gaa Glu	1044
agc Ser	aca Thr	gaa Glu	tca Ser 290	gat Asp	aac Asn	aat Asn	aaa Lys	tat Tyr 295	tgg Trp	ctg Leu	gtg Val	aag Lys	aac Asn 300	agc Ser	tgg Trp	1092
ggt Gly	gaa Glu	gaa Glu 305	tgg Trp	GJ Y ggc	atg Met	ggt Gly	ggc Gly 310	tac Tyr	gta Val	aag Lys	atg Met	gcc Ala 315	aaa Lys	gac Asp	cgg Arg	1140

gctggtggac ggtgatgagg aaggacttga ctggggatgg cgcatgcatg ggaggaattc 1248
525-35-6 55-54-55
atcttcagtc taccagecce egetgtgteg gatacacact egaatcattg aagateegag 1308
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ctataaatag gtttatatta ttgattcact tactgacttt gcattttcgt ttttaaaagg 1428
atgtataaat ttttacctgt ttaaataaaa tttaatttca aatgtaaaaa aaaaaaaa 1486

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<211> 799

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (123)..(749)

<400> 50

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gccactgacc accgtggaga agcccggggg aggggaggtg ctttctggct gcacactgac 120

atg ttg ggg tgc cag ggc agg atg tac acg ctg ctg tcg ggc ttg

Met Leu Gly Cys Gln Gly Arg Met Tyr Thr Leu Leu Ser Gly Leu

tac aag tac atg ttt cag aag gac gag tac tgc atc ctg atc ctg ggc

Tyr Lys Tyr Met Phe Gln Lys Asp Glu Tyr Cys Ile Leu Ile Leu Gly

20 25 30

ctg gac aat gct ggg aag acg acc ttc ctg gag cag tcg aaa acc cga
Leu Asp Asn Ala Gly Lys Thr Thr Phe Leu Glu Gln Ser Lys Thr Arg
35 40 45

ttt aac aag aac tac aag ggg atg agt cta tcc aaa atc acc acc acc Phe Asn Lys Asn Tyr Lys Gly Met Ser Leu Ser Lys Ile Thr Thr Thr 50 55 60

gtg ggc cta aac atc ggc act gtg gat gtg gga aag gct cgg ctc atg
Val Gly Leu Asn Ile Gly Thr Val Asp Val Gly Lys Ala Arg Leu Met
65 70 75

ttc tgg gac tta gga ggg cag gaa gag ctg cag tct ttg tgg gac aag

Phe Trp Asp Leu Gly Gly Gln Glu Glu Leu Gln Ser Leu Trp Asp Lys

80 85 90 95

tat tat gcg gag tgt cac ggc gtc atc tac gtc att gac tcc acc gac

Tyr Tyr Ala Glu Cys His Gly Val Ile Tyr Val Ile Asp Ser Thr Asp

100 105 110

gag gag agg ctg gct gag tcc aag cag gcg ttt gag aag gtg gtg acc 503

Glu	Glu	Arg	Leu 115	Ala	Glu	Ser	ГÀЗ	Gln 120	Ala	Phe	Glu	Lys	Val 125	Val	Thr	
agc Ser	gag Glu	gcg Ala 130	ctg Leu	tgc Cys	ggt Gly	gtc Val	ccc Pro 135	gtc Val	ttg Leu	gtg Val	ctg Leu	gcc Ala 140	aac Asn	aag Lys	cag Gln	551
gat Asp	gtg Val 145	gag Glu	acg Thr	tgc Cys	ctc Leu	tca Ser 150	atc Ile	cct Pro	gac Asp	atc Ile	aag Lys 155	acg Thr	gcc Ala	ttc Phe	agc Ser	599
gac Asp 160	tgc Cys	acc Thr	agc Ser	aag Lys	atc Ile 165	ggc Gly	agg Arg	cga Arg	gat Asp	tgc Cys 170	ctg Leu	acc Thr	cag Gln	gcc Ala	tgc Cys 175	647
tcg Ser	gcc Ala	ctc Leu	aca Thr	ggc Gly 180	aaa Lys	gjà aaa	gtg Val	cgc Arg	gag Glu 185	ggc Gly	atc Ile	gag Glu	tgg Trp	atg Met 190	gtg Val	695 [.]
aag Lys	tgt Cys	gtc Val	gtg Val 195	cgg Arg	aat Asn	gtg Val	cac His	cgg Arg 200	ccg Pro	ccg Pro	cgg Arg	cag Gln	agg Arg 205	gac Asp	atc Ile	743
acg Thr	tag	gcg	agco	ccg (gctt	gccc	g to	cggg	jacgg	ctg	gtco	ecct	ggtg	gctgg	gag	799

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														tgt Cys		366
														ttc Phe		414
														atc Ile		462
														gag Glu		510
			_		_				_			_		cgt Arg 130		558
_		_		_										ttt Phe		606
cca Pro	tac Tyr	tgg Trp 150	ggg ggg	cag Gln	aca Thr	cta Leu	tgt Cys 155	ttc Phe	cgg Arg	gtg Val	ctg Leu	gtg Val 160	cct Pro	gaa Glu	ctt Leu	654
														cga Arg		702
														caa Gln		750
	_				_	_			-			_		cgc Arg 210		798
														GJA aaa		846
	tcc Ser	tga	ggt	gggc	att	tcac	ggg (aagg	gttg	gt g	tgct	ggct	t ta	gacg	ggga	902
gaa	acat	ctg	gaag	gatg	ct c	gaga	gaac	a aa	tgga	ggtg	gtg	aaaa	tca	agct	ttggat	962
tgt	gcat	tcc	tagg	caca	aa a	ttac	ctca	t tc	ttcc	taac	aag	caat	ctg	ggac	ctgatt	1022
ttc	cacc	ttt	tttc	tctt	tt c	ttcc	cttc	c tt	tgtt	ttca	taa	gcct	ttg	gtat	ctttcc	1082
tgc	cctt	ttc	cttt	gtgt	ac t	ctat	actg	g ag	ttcc	cttc	ttc	ctct	tgc	tgta	ggctca	1142
atc	ccat	acc	gaca	tcta	ca a	ctaa	tctt	t cc	catc	aact	ctg	tgtg	aag	gcag	gttgca	1202
act	agaa	att	caga	3333	ct t	ggaa	taga	g aa	acct	aaag	aag	catc	atc	ccct	ccatcc	1262
cca	actt	cct	caaa	gccc	aa a	gcca	aggg	a ag	gata	aatc	aag	gctc	aag	gctt	ccccag	1322

caaagattag ggaaagagac ttgaccccag gactgtacta cgactcttaa gagaacactg

cacagcactc	aaagtccccc	actggactgc	: ttcctcctta	gccccactgg	tataaataca	1442
tctctctcca	atttggcttc	aa				1464
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				tggtagcagc		120
				tgagaaggct		180
				cctcagcttg		240
				tetectgete		300
tgcctgtggc	aggcagcacc	ttgagccaac	aggaaccatt		a ggc cca g Gly Pro	355
ggg cag gca Gly Gln Ala 5	ı Asp Cys Al	a gtg gcc a a Val Ala : 0	att ggg cgg Ile Gly Arg 15	ccc ctc ggg Pro Leu Gly	gag gtg Glu Val 20	403
gtg acc cto Val Thr Lei	cgc gtc ct Arg Val Le 25	t gag agt (u Glu Ser (tct ctc aac Ser Leu Asn 30	tgc agt gcg Cys Ser Ala	ggg gac Gly Asp 35	451
atg ttg ctg Met Leu Leu	ctt tgg gg Leu Trp Gl 40	c cgg ctc a y Arg Leu 1	acc tgg agg Thr Trp Arg 45	aag atg tgc Lys Met Cys 50	agg aag Arg Lys	499
ctg ttg gad Leu Leu Asp 55	Met Thr Ph	c agc tcc a e Ser Ser I 60	aag acc aac Lys Thr Asn	acg ctg gtg Thr Leu Val 65	gtg agg Val Arg	547
cag cgc tgc Gln Arg Cys 70	ggg cgg cc Gly Arg Pr	a gga ggt g o Gly Gly 0 75 ,	ggg gtg ctg Gly Val Leu	ctg cgg tat Leu Arg Tyr 80	ggg agc Gly Ser	595
cag ctt gct Gln Leu Ala 85	cct gaa ac Pro Glu Th 9	r Phe Tyr <i>F</i>	aga gaa tgt Arg Glu Cys 95	gac atg cag Asp Met Gln	ctc ttt Leu Phe 100	643
ggg ccc tgg Gly Pro Trp	ggt gaa at Gly Glu Il 105	c gtg agc o e Val Ser F	ecc tcg ctg Pro Ser Leu 110	agt cca gcc Ser Pro Ala	acg agt Thr Ser 115	691

aat gca ggg ggc tgc cgg ctc ttc att aat gtg gct ccg cac gca cgg Asn Ala Gly Gly Cys Arg Leu Phe Ile Asn Val Ala Pro His Ala Arg 120 125 130	739
att gcc atc cat gcc ctg gcc acc aac atg ggc gct ggg acc gag gga Ile Ala Ile His Ala Leu Ala Thr Asn Met Gly Ala Gly Thr Glu Gly 135 140 145	787
gcc aat gcc agc tac atc ttg atc cgg gac acc cac agc ttg agg acc Ala Asn Ala Ser Tyr Ile Leu Ile Arg Asp Thr His Ser Leu Arg Thr 150 155 160	835
aca gcg ttc cat ggg cag cag gtg ctc tac tgg gag tca gag agc agc Thr Ala Phe His Gly Gln Gln Val Leu Tyr Trp Glu Ser Glu Ser Ser 165 170 175 180	883
cag gct gag atg gag ttc agc gag ggc ttc ctg aag gct cag gcc agc Gln Ala Glu Met Glu Phe Ser Glu Gly Phe Leu Lys Ala Gln Ala Ser 185 190 195	931
ctg cgg ggc cag tac tgg aca ctc caa tca tgg gta ccg gag atg cag Leu Arg Gly Gln Tyr Trp Thr Leu Gln Ser Trp Val Pro Glu Met Gln 200 205 210	979
gac cct cag tcc tgg aag gga aag gaa gga acc tga gggt cattgaacat Asp Pro Gln Ser Trp Lys Gly Lys Glu Gly Thr 215 220	1029
ttgttccgtg tctggccagc cctggagggt tgacccctgg tctcagtgct ttccaattcg	1089
aactttttcc aatcttaggt atctacttta gagtcttctc caatgtccaa aaggctaggg	1149
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<213> Homo sapiens
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<221> CDS
<222> (375)..(596)
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cacgggcaat gccttgggtc ctagaccgtg ggctgggagc cacataaagg tcttgggtac 180

tcttaggagt	t aggtgeeegg gggageaege eeaggaeata teaggtteee teaccaaget	240
tageceecte	c tgeeetetgt tgagteteet gagteeettt ggagteeete tettgeteee	300
atgcagacaa	a ctggaagcag gagctgacaa aattcatcag ccccgaccag ctgcctgtgg	360
agtttggggg	g gacc atg act gac ccc gat ggc aac ccc aag tgc ctg acc Met Thr Asp Pro Asp Gly Asn Pro Lys Cys Leu Thr 1 5 10	410
ras ile As	ac tac ggg ggt gag gtg ccc aag agc tac tac ctg tgc aag sn Tyr Gly Gly Glu Val Pro Lys Ser Tyr Tyr Leu Cys Lys 15 20 25	458
cag gtg ag Gln Val Ar 30	gg ctg cag tat gag cac acg agg tcc gtg ggc cgc ggc tcc rg Leu Gln Tyr Glu His Thr Arg Ser Val Gly Arg Gly Ser 35 40	506
tcc ctg ca Ser Leu Gl 45	ag gtg gag aac gag atc ctg ttc ccg ggc tgt gtg ctc aga In Val Glu Asn Glu Ile Leu Phe Pro Gly Cys Val Leu Arg 50 55 60	554
tgt cct ga Cys Pro Gl	ng gtt tta caa cac cta cag cct ggt tca ttc taa acgcatc nu Val Leu Gln His Leu Gln Pro Gly Ser Phe 65 70	603
agctacaccg	g tggaggtact gctcccagac caaaccttca tggagaagat ggagaaattc	663
taggtgaacc	tcatggtccc cacaccctcc tctttgatct ctgaatccac aatgagttca	723
cagcetteec	tggccagacc ctgttcaacc tctcaggaac agggattcta caacagcagg	783
tcacagccta	tgcatcacag ctggcccact cctcaagaac ggctgggaca gtgtcctagt	843
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gacctcaagc	tcagcaaaac cccaggcttt g	934
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	Homo sapiens	
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taccggtccg gaattcccgg gtcgacgatt tcgtggcttg ggtaaaa atg gct gaa 56
Met Ala Glu

tat tta gct tcg ata ttc ggg act gag aag gac aag gtt aac tgc tct
Tyr Leu Ala Ser Ile Phe Gly Thr Glu Lys Asp Lys Val Asn Cys Ser

5 10 15

ttt tac ttt aag atc ggg gtc tgc cgg cac ggg gac cgg tgc tcc cgg
Phe Tyr Phe Lys Ile Gly Val Cys Arg His Gly Asp Arg Cys Ser Arg

20					25					30					35	
	_		_	ccg Pro 40			_	_					_		_	200
				gag Glu												248
_				ggc Gly		_		_	_						_	296
			_	gtg Val	_	_		_		_					_	344
_				aat Asn	_				_		_			_		392
tgc Cys	ggc Gly	cca Pro	ttt Phe	ccc Pro 120	aga Arg	acc Thr	tcc Ser	aga Arg	ggc Gly 125	agc Ser	tct Ser	atg Met	ggc Gly	130 Gly 999	gac Asp	440
				cac His												488
				ggt Gly												536
				tta Leu												584
	_			tca Ser	_											632
		_		tcc Ser 200		_	taa	tet	gttca	agc a	atgga	agac	et to	ettei	accg	686
ccc	ctgto	ctt a	aata													700

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<211> 855

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (48)..(773)

<400> 55

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tat Tyr	tta Leu 5	gct Ala	tcg Ser	ata Ile	ttc Phe	10 GJ ^A aaa	act Thr	gag Glu	aag Lys	gac Asp	aag Lys 15	gtt Val	aac Asn	tgc Cys	tct Ser		104
ttt Phe 20	tac Tyr	ttt Phe	aag Lys	att Ile	ggc Gly 25	gcc Ala	tgc Cys	cgg Arg	cac His	30 Gly 399	gac Asp	cgg Arg	tgc Cys	tcc Ser	cga Arg 35		152
ctt Leu	cac His	aac Asn	aaa Lys	ccg Pro 40	act Thr	ttc Phe	agc Ser	cag Gln	acc Thr 45	ata Ile	gtc Val	ctg Leu	ctc Leu	aac Asn 50	ttg Leu		200
tac Tyr	cgg Arg	aat Asn	cca Pro 55	cag Gln	aac Asn	aca Thr	gcc Ala	caa Gln 60	act Thr	gca Ala	gac Asp	gga Gly	tca Ser 65	cac His	tgt Cys		248
cat His	gtg Val	agc Ser 70	gac Asp	gtg Val	gag Glu	gtg Val	cag Gln 75	gag Glu	cac His	tat Tyr	gat Asp	agc Ser 80	ttc Phe	ttc Phe	gag Glu		296
gag Glu	gtg Val 85	ttc Phe	aca Thr	gaa Glu	ctg Leu	cag Gln 90	gag Glu	aag Lys	tat Tyr	glà aaa	gag Glu 95	att Ile	gaa Glu	gag Glu	atg Met		344
aat Asn 100	gtg Val	tgc Cys	gac Asp	aac Asn	ctt Leu 105	Gl ^y aaa	gac Asp	cac His	ctc Leu	gtg Val 110	ggc ggc	aac Asn	gtc Val	tat Tyr	gtc Val 115		392
aag Lys	ttc Phe	cgg Arg	agg Arg	gag Glu 120	gag Glu	gat Asp	gga Gly	gag Glu	cgg Arg 125	gcc Ala	gtg Val	gct Ala	gaa Glu	ctc Leu 130	agt Ser		440
aac Asn	cgc Arg	tgg Trp	ttc Phe 135	aac Asn	Gly 333	cag Gln	gct Ala	gtg Val 140	cac His	gjà aaa	aat Asn	gta Val	ccc Pro 145	gag Glu	gtg Val		488
gct Ala	tct Ser	gca Ala 150	act Thr	tca Ser	Cya tgc	atc Ile	tgc Cys 155	ggc Gly	cca Pro	ttt Phe	ccc Pro	aga Arg 160	acc Thr	tcc Ser	aga Arg		536
Gly	agc Ser 165	tct Ser	atg Met	Gly	gjå aaa	gac Asp 170	cca Pro	gly	gca Ala	ggt Gly	cac His 175	ccc Pro	cga Arg	ggt Gly	tcc Ser		584
ata Ile 180	ctg Leu	gcc Ala	acc Thr	atc Ile	ccc Pro 185	gag Glu	aga Arg	gga Gly	acc Thr	atc Ile 190	gtt Val	gtt Val	ccc Pro	ctg Leu	atc Ile 195		632
act Thr	ggc	atg Met	gcc Ala	gct Ala 200	tct Ser	gag Glu	gcc Ala	ctg Leu	gcc Ala 205	ccc Pro	tta Leu	ccc Pro	ttc Phe	acc Thr 210	ccc Pro		680
	agg Arg																728
ctc	tcc	tgc	ccc	atc	ctt	ccc	agg	ctc	ccg	ggc	tcc	ata	atg	taa	tct		776

Leu Ser Cys Pro Ile Leu Pro Arg Leu Pro Gly Ser Ile Met 230 235 240

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<211> 3068

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (128)..(2512)

<400> 56

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Met Leu Cys Gly Arg Trp Arg Cys Arg Arg Pro Pro Glu

gag ccc cca gtg gcc gcc cag gtc gca gcc caa gtc gcg gcg ccg gtc 217
Glu Pro Pro Val Ala Ala Gln Val Ala Ala Gln Val Ala Ala Pro Val

20 25 30

gct ctc ccg tcc ccg ccg act ccc tcc gat ggc ggc acc aag agg ccc 265
Ala Leu Pro Ser Pro Pro Thr Pro Ser Asp Gly Gly Thr Lys Arg Pro

35
40
45

ggg ctg cgg gcg ctg aag aag atg ggc ctg acg gag gac gtg 313
Gly Leu Arg Ala Leu Lys Lys Met Gly Leu Thr Glu Asp Glu Asp Val
50 55 60

cgc gcc atg ctg cgg ggc tcc cgg ctc cgc aag atc cgc tcg cgc acg

Arg Ala Met Leu Arg Gly Ser Arg Leu Arg Lys Ile Arg Ser Arg Thr

65

70

75

tgg cac aag gag cgg ctg tac cgg ctg cag gag gac ggc ctg agc gtg
Trp His Lys Glu Arg Leu Tyr Arg Leu Gln Glu Asp Gly Leu Ser Val
80 85 90

tgg ttc cag cgg cgc atc ccg cgt gcg cca tcg cag cac atc ttc ttc

Trp Phe Gln Arg Arg Ile Pro Arg Ala Pro Ser Gln His Ile Phe Phe

95 100 105 110

gtg cag cac atc gag gcg gtc cgc gag ggc cac cag tcc gag ggc ctg 505 Val Gln His Ile Glu Ala Val Arg Glu Gly His Gln Ser Glu Gly Leu 115 120 125

cgg cgc ttc ggg ggt gcc ttc gcg cca gcg cgc tgc ctc acc atc gcc
Arg Arg Phe Gly Gly Ala Phe Ala Pro Ala Arg Cys Leu Thr Ile Ala
130
135
140

ttc aag ggc cgc cgc aag aac ctg gac ctg gcg ccc acg gct gag 601

Phe	Lys	Gly 145	Arg	Arg	ГУв	Asn	Leu 150	Asp	Leu	Ala	Ala	Pro 155		Ala	Glu	
gaa Glu	gcg Ala 160	Gln	cgc Arg	tgg Trp	gtg Val	cgc Arg 165	ggt Gly	ctg Leu	acc Thr	aag Lys	ctc Leu 170	Arg	gcg Ala	cgc Arg	ctg Leu	649
gac Asp 175	Ala	atg Met	agc Ser	cag Gln	cgc Arg 180	gag Glu	cgg Arg	cta Leu	gac Asp	cac His 185	tgg Trp	atc Ile	cac His	tcc Ser	tat Tyr 190	697
ctg Leu	cac His	cgg Arg	gct Ala	gac Asp 195	tcc Ser	aac Asn	cag Gln	gac Asp	agc Ser 200	aag Lys	atg Met	agc Ser	ttc Phe	aag Lys 205	gag Glu	745
atc Ile	aag Lys	agc Ser	ctg Leu 210	ctg Leu	aga Arg	atg Met	gtc Val	aac Asn 215	gtg Val	gac Asp	atg Met	aac Asn	gac Asp 220	atg Met	tac Tyr	793
gcc Ala	tac Tyr	ctc Leu 225	ctc Leu	ttc Phe	aag Lys	gag Glu	tgt Cys 230	gac Asp	cac His	tcc Ser	aac Asn	aac Asn 235	gac Asp	cgt Arg	cta Leu	841
Glu	Gly 240	Ala	Glu	Ile	Glu	gag Glu 245	Phe	Leu	Arg	Arg	Leu 250	Leu	Lys	Arg	Pro	88 <i>9</i>
gag Glu 255	ctg Leu	gag Glu	gag Glu	atc Ile	ttc Phe 260	cat His	cag Gln	tac Tyr	tcg Ser	ggc Gly 265	gag Glu	gac Asp	ege Arg	gtg Val	ctg Leu 270	937
agt Ser	gcc Ala	cct Pro	gag Glu	ctg Leu 275	ctg Leu	gag Glu	ttc Phe	ctg Leu	gag Glu 280	gac Asp	cag Gln	ggc	gag Glu	gag Glu 285	ggc ggc	985
gcc Ala	aca Thr	ctg Leu	gcc Ala 290	cgc Arg	gcc Ala	cag Gln	cag Gln	ctc Leu 295	att Ile	cag Gln	acc Thr	tat Tyr	gag Glu 300	ctc Leu	aac Asn	1033
Glu	Thr	Ala 305	ГÀв	Gln	His	gag Glu	Leu 310	Met	Thr	Leu	Asp	Gly 315	Phe	Met	Met	1081
Tyr	120	Leu	Ser	Pro	Glu	325 325	Ala	Ala	Leu	qaA	Asn 330	Thr	His	Thr	Cys	1129
Val 335	Phe	Gln	Asp	Met	Asn 340	cag Gln	Pro	Leu	Ala	His 345	Tyr	Phe	Ile	Ser	<i>S</i> er 350	1177
tcc Ser	Cac His	aac Asn	acc Thr	tat Tyr 355	ctg Leu	act Thr	gac Asp	tcc Ser	cag Gln 360	atc Ile	gjå aaa	gly aaa	ccc Pro	agc Ser 365	agc Ser	1225
Thr	Glu	Ala	Tyr 370	Val	Arg	tac Tyr	Сув	Ser 375	Arg	Gly	Ala	Phe	Ala 380	Gln	Gly	1273
tgc Cys	cgc Arg	tgc Cys	gtg Val	gag Glu	ctg Leu	gac Asp	tgc Cys	tgg Trp	gag Glu	gly ggg	cca Pro	gga Gly	ggg ggg	gag Glu	ccc Pro	1321

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gtc atc Val Ile 400												_	1369
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gtc atc Val Ile													1465
atg gcc (Met Ala													1513
gcg ctg													1561
aag ggc Lys Gly 480													1609
gag gat Glu Asp 495			Ser										1657
gag gag Glu Glu													1705
aag cag Lys Gln													1753
acc cgc Thr Arg		_			_			_				_	1801
cag gtc Gln Val 560	Ser Ser	Leu Ser	Glu 565	Arg	Lys	Ala	Lys	Lys 570	Leu	Ile	Arg	Glu	1849
gca ggg Ala Gly 575	Asn Ser	Phe Val	Arg	His	Asn	Ala	Arg 585	Gln	Leu	Thr	Arg	Val 590	1897
tac ccg Tyr Pro	Leu Gly	Leu Arg	Met	Asn	Ser	Ala 600	Asn	Tyr	Ser	Pro	Gln 605	Glu	1945
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ggc tac Gly Tyr													2041

Cys	Gly 640	Tyr	Val	Leu	aaa Lys	Pro 645	gcc Ala	tgc Cys	ctg Leu	Arg	caa Gln 650	cct Pro	gac Asp	tcg Ser	acc Thr	2089
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gtg Val	ctg Leu	act Thr	gca Ala	cag Gln 675	cag Gln	ctg Leu	ccc Pro	aag Lys	ctg Leu 680	aat Asn	gcc Ala	gag Glu	aag Lys	cca Pro 685	cac His	2185
tcc Ser	att Ile	gtg Val	gac Asp 690	ccc Pro	ctg Leu	gtg Val	cgc Arg	att Ile 695	gag Glu	atc Ile	cat His	61 <i>\</i> 333	gtg Val 700	ccc Pro	gca Ala	2233
gac Asp	tgt Cys	gcc Ala 705	cgg Arg	cag Gln	gag Glu	act Thr	gac Asp 710	tac Tyr	gtg Val	ctc Leu	aac Asn	aat Asn 715	Gly ggc	ttc Phe	aac Asn	2281
ccc Pro	cgc Arg 720	tgg Trp	G1A aaa	cag Gln	acc Thr	ctg Leu 725	cag Gln	ttc Phe	cag Gln	ctg Leu	cgg Arg 730	gct Ala	ccg Pro	gag Glu	ctg Leu	2329
gca Ala 735	ctg Leu	gtc Val	cgg Arg	ttt Phe	gtg Val 740	gtg Val	gaa Glu	gat Asp	tat Tyr	gac Asp 745	gcc Ala	acc Thr	tcc Ser	ccc Pro	aat Asn 750	2377
gac Asp	ttt Phe	gtg Val	ggc Gly	cag Gln 755	ttt Phe	aca Thr	ctg Leu	cct Pro	ctt Leu 760	agc Ser	agc Ser	cta Leu	aag Lys	caa Gln 765	el ^a aaa	2425
tac Tyr	cgc Arg	cac His	ata Ile 770	cac His	ctg Leu	ctt Leu	tcc Ser	aag Lys 775	gac Asp	GJ y aga	gcc Ala	tca Ser	ctg Leu 780	tca Ser	cca Pro	2473
gcc Ala	acg Thr	ctc Leu 785	ttc Phe	atc Ile	caa Gln	atc Ile	cgc Arg 790	atc Ile	cag Gln	cgc Arg	tcc Ser	tga	gggc	ccac	ct	2522
cact	cgcc	tt g	gggt	tate	ıc ga	gtgc	cagt	сса	cato	ccc	tgca	gago	cc t	ctcc	tcctc	2582
tgga	gtca	gg t	ggtg	ggag	rt ac	cago	cccc	cag	ccca	ccc	actt	ggcc	ca c	tcag	cccat	2642
tcac	cagg	icg c	tggt	ctca	c ct	gggt	gctg	agg	gctg	cct	gggc	ccct	cc t	gaag	aacag	2702
aaag	gtgt	tc a	tgtg	actt	c ag	tgag	ctcc	aac	cctg	9 99	ccct	gaga	tg g	cccc	agctc	2762
ctct	tgtc	ct c	agcc	cacc	c ct	catt	gtga	ctt	atga	gga	gcaa	gcct	gt t	gctg	ccagg	2822
agac	ttgg	gg a	gcag	gaca	c tt	gtgg	gccc	tca	gttc	ccc	tctg	tcct	cc c	gtgg	gccat	2882
ccca	gcct	cc t	tccc	ccag	a gg	agcg	cagt	cac	tcca	ctt	ggcc	ccga	cc c	cgag	cttag	2942
															acctg	3002
agct	cccc	tt c	cctt	ctca	a ag	caag	aagg	gag	cgct	gag	gcat	gaag	cc c	tggg	gaaac	3062
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gccctgtgcc	cagtgacccc actagctttt ccctctactt teceegeetg getgtgetee	180
ccttgattcg	tgcctattgg ccgtgcccat agtctctccc aagctcaaag ttcacctctt	240
tctccagatc	ccctggggtc cccaagcctg actcagtgta tctggggggg tcccttctga	300
gcccacgcac	e cgacccaget cetetteeet geagttgtgg ce atg geg get gtg Met Ala Ala Val 1	354
	g ctc agt gcc atg ggc ttc act gcg gcg gga atc gcc tcg l Leu Ser Ala Met Gly Phe Thr Ala Ala Gly Ile Ala Ser 10 15 20	402
	a gca gcc aag atg atg tcc gca gca gcc att gcc aac ggg e Ala Ala Lys Met Met Ser Ala Ala Ala Ile Ala Asn Gly 25 30 35	4 50
	t tot gog ggg ago otg gtg got act otg cag too gtg ggg il Ser Ala Gly Ser Leu Val Ala Thr Leu Gln Ser Val Gly 40 45 50	498
Ala Ala Gl	ga ctc tcc aca tca tcc aac atc ctc ctg gcc tct gtt ggg .y Leu Ser Thr Ser Ser Asn Ile Leu Leu Ala Ser Val Gly .5 60 65	546
	eg ggg gcc tgc ttg ggg aat tca cct tct tct tct ctc cca eu Gly Ala Cys Leu Gly Asn Ser Pro Ser Ser Ser Leu Pro 75 80	594
	cc gag gct aaa gaa gat gag gca aga gaa aat gta ccc caa co Glu Ala Lys Glu Asp Glu Ala Arg Glu Asn Val Pro Gln 90 95 100	642
	ct cca aaa ccc cca ctc aag tca gag aaa cat gag gaa taa co Pro Lys Pro Pro Leu Lys Ser Glu Lys His Glu Glu 105 110 115	690
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cgg gtg cag ctg gga cac agc aat gag atg agg ctc cac ggc gtc ccg Arg Val Gln Leu Gly His Ser Asn Glu Met Arg Leu His Gly Val Pro 190 195 200	745
tec gag gge cet gee cae ate eee eet gge age eee eea gte tet gee Ser Glu Gly Pro Ala His Ile Pro Pro Gly Ser Pro Pro Val Ser Ala 205 210 215	793
act gct gcc ggc cca gaa gct tcg ttt gaa gca aga att ccc agt cca Thr Ala Ala Gly Pro Glu Ala Ser Phe Glu Ala Arg Ile Pro Ser Pro 220 225 230 235	841
gga act cac cct gag ggg gaa gcc gcc cag aga atc cac atg aaa tcg Gly Thr His Pro Glu Gly Glu Ala Ala Gln Arg Ile His Met Lys Ser 240 245 250	889
tgc ttt ctc gag gac gcc acc atc ggc aac agc aac aaa atg tct atc Cys Phe Leu Glu Asp Ala Thr Ile Gly Asn Ser Asn Lys Met Ser Ile 255 260 265	937
cag ccc agg ggt ggc tgg ccc agg agg agt cgc agg gtc tgg aga ggg Gln Pro Arg Gly Gly Trp Pro Arg Arg Ser Arg Arg Val Trp Arg Gly 270 275 280	985
gga gcc agg gga gga cgc agt tgc tgc ctt cac tga agtc ttgaacccct Gly Ala Arg Gly Gly Arg Ser Cys Cys Leu His 285 290	1035
caaagtcatt catgaaattt ggaatcaact tcttccagac tcctgtgaat gttgatagtt	1095
tgacctcctc ccatgaatca caaatgttct taacggcatg tagattggtg atcttttcca	1155
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Met

tca gtc cgt tct aaa ttg cca aat tct cca gca gca tct tct cat ccc 165
Ser Val Arg Ser Lys Leu Pro Asn Ser Pro Ala Ala Ser Ser His Pro

aag ctc aag tct tca aaa ggc ata acg aag aaa ccg cag gct cct tca
Lys Leu Lys Ser Ser Lys Gly Ile Thr Lys Lys Pro Gln Ala Pro Ser

138

20

25

30

aac Asn	aat Asn 35	ı Ala	tca Ser	tct Ser	tca Ser	ctt Leu 40	Ala	tca Ser	tta Leu	aat Asn	Pro 45	Val	Gly	aaa Lys	aac Asn	261	L
act Thr 50	Ser	tca Ser	cca Pro	gct Ala	tta Leu 55	Pro	aga Arg	act Thr	gca Ala	cct Pro 60	Сув	ata Ile	tct Ser	gag Glu	tca Ser 65	309	,
ccg Pro	aga Arg	aaa Lys	tgt Cys	att Ile 70	Ser	tcc Ser	Pro	aat Asn	acc Thr 75	Pro	aag Lys	gcc Ala	aag Lys	gtt Val 80	Ile	357	,
cca Pro	gcc Ala	cag Gln	aat Asn 85	Ser	gca Ala	gat Asp	ctg Leu	Pro 90	Glu	tcc Ser	aca Thr	ctt Leu	ttg Leu 95	Pro	aat Asn	405	,
aag Lys	tgt Cys	tca Ser 100	Gly	aaa Lys	act Thr	caa Gln	cct Pro 105	Lys	tat Tyr	ttg Leu	aaa Lys	cat His 110	aac Asn	cat His	att Ile	453	
tct Ser	tcc Ser 115	aga Arg	gat. Asp	aat Asn	gca Ala	gta Val 120	tct Ser	cac His	tta Leu	gct Ala	gca Ala 125	cat His	tca Ser	aat Asn	tca Ser	501	
tcc Ser 130	tca Ser	aaa Lys	tgt Cys	ccc Pro	aag Lys 135	ctg Leu	cct Pro	aaa Lys	gca Ala	aat Asn 140	ata Ile	cct Pro	gta Val	aga Arg	cct Pro 145	549	
aaa Lys	cct Pro	tct Ser	ttc Phe	cag Gln 150	tcc Ser	tct Ser	gca Ala	aaa Lys	atg Met 155	aca Thr	aaa Lys	acc Thr	agt Ser	tcc Ser 160	aaa Lys	597	
acc Thr	ata Ile	gcc Ala	acg Thr 165	ggt Gly	cta Leu	gga Gly	aca Thr	cag Gln 170	tct Ser	caa Gln	cca Pro	tcc Ser	gat Asp 175	gga Gly	gcc Ala	645	
cca Pro	caa Gln	gca Ala 180	aag Lys	cca Pro	gtc Val	cca Pro	gca Ala 185	cag Gln	aaa Lys	ctt Leu	aaa Lys	tcg Ser 190	gcc Ala	ttg Leu	aat Asn	693	
tta Leu	aat Asn 195	cag Gln	cca Pro	gtt Val	tct Ser	gtg Val 200	tcc Ser	tca Ser	gtt Val	tct Ser	cct Pro 205	gta Val	aaa Lys	gcc Ala	aca Thr	741	
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cct Pro	ggc Gly	cgt Arg	acc Thr 245	cca Pro	ctg Leu	tcc Ser	atc Ile	gtg Val 250	agc Ser	cta Leu	ccc Pro	cag Gln	tct Ser 255	tct Ser	acc ' Thr	885	
aaa Lys	aca Thr	caa Gln 260	act Thr	gca Ala	ccg Pro	Lys	tca Ser 265	gca Ala	cag Gln	act Thr	gtc Val	gct Ala 270	aag Lys	agc Ser	cag Gln	933	

cat tca a His Ser T 275											981
agg aaa c Arg Lys F 290			-		Ala A	_		_			1029
cct act g Pro Thr A	Ala Lys I	_	-	_	_			_	_		1077
gga agt a Gly Ser I	-	_		aa atad	catact	c attat	aaaa	a aa	ıaaaa	ıaa	1129

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60

108

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Met Ala Pro Thr Leu Phe Gln Lys Leu Phe Ser Lys Arg

acc ggg ctg ggc gcc cgc ggc cgc gac gcc cgg gac cca gat tgc ggg
Thr Gly Leu Gly Ala Pro Gly Arg Asp Ala Arg Asp Pro Asp Cys Gly
15 20 25

ttc agt tgg cct tta cca gag ttt gat cca agc cag att cga ctg att

Phe Ser Trp Pro Leu Pro Glu Phe Asp Pro Ser Gln Ile Arg Leu Ile

30 35 40 45

gta tat caa gac tgt gaa aga cga ggg aga aat gtt ttg ttt gac tcc 252
Val Tyr Gln Asp Cys Glu Arg Arg Gly Arg Asn Val Leu Phe Asp Ser

agt gtt aag aga aga aat gag gac ata tca gta tcg gac tta aat act 300 Ser Val Lys Arg Arg Asn Glu Asp Ile Ser Val Ser Asp Leu Asn Thr
65 70 75

att tat tct tat ctt cat gga atg gaa ata tta tca aat ctc agg gaa 348

Ile Tyr Ser Tyr Leu His Gly Met Glu Ile Leu Ser Asn Leu Arg Glu

80 85 90

cat cag ctt aga tta atg tct gca aga gca cgc tat gag aga tac agt
His Gln Leu Arg Leu Met Ser Ala Arg Ala Arg Tyr Glu Arg Tyr Ser
95 100 105

ggc Gly 110	aat Asn	cag Gln	gtt Val	ctc Leu	ttt Phe 115	tgt Cys	tca Ser	gaa Glu	acg Thr	att Ile 120	gcc Ala	aga Arg	tgt Cys	tgg Trp	tat Tyr 125	444
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cct Pro	tgc Cys	agt Ser	ttt Phe 145	ggt Gly	aag Lys	cag Gln	ttt Phe	gga Gly 150	gga Gly	aaa Lys	aga Arg	gga Gly	tgt Cys 155	gat Asp	tgt Cys	540
ctt Leu	gta Val	tta Leu 160	gag Glu	cct Pro	tca Ser	gaa Glu	atg Met 165	att Ile	gtg Val	gta Val	gag Glu	aat Asn 170	gcc Ala	aaa Lys	gat Asp	588
aat Asn	gaa Glu 175	gat Asp	agt Ser	att Ile	cta Leu	caa Gln 180	aga Arg	gaa Glu	att Ile	cct Pro	gcc Ala 185	aga Arg	caa Gln	tcc Ser	cga Arg	636
aga Arg 190	aga Arg	ttt Phe	cgg Arg	aaa Lys	att Ile 195	aac Asn	tat Tyr	aaa Lys	gga Gly	gag Glu 200	cgc Arg	caa Gln	acc Thr	att Ile	act Thr 205	684
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tta Leu	tct Ser 255	gat Asp	atc Ile	tat Tyr	cag Gln	gct Ala 260	acg Thr	gag Glu	agt Ser	gag Glu	gta Val 265	gga Gly	gat Asp	gta Val	gat Asp	876
ttg Leu 270	aca Thr	cgt Arg	ctt Leu	cca Pro	gaa Glu 275	gga Gly	cct Pro	gtt Val	gat Asp	tct Ser 280	gag Glu	gat Asp	gac Asp	gaa Glu	gag Glu 285	924
gaa Glu	gat Asp	gaa Glu	gag Glu	att Ile 290	gat Asp	cga Arg	aca Thr	gat Asp	cca Pro 295	ttg Leu	cag Gln	gly ggg	cga Arg	gat Asp 300	ctt Leu	972
gtt Val	cga Arg	gaa Glu	tgt Cys 305	ctt Leu	gaa Glu	aaa Lys	gaa Glu	cct Pro 310	gca Ala	gac Asp	aaa Lys	act Thr	gat Asp 315	gat Asp	gac Asp	1020
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gtg	gta	gag	cag	gct	gga	gct	att	att	ctt	gaa	gat	999	caa	gag	ctt	1164

Val 350	Val	Glu	Gln	Ala	Gly 355	Ala	Ile	Ile	Leu	Glu 360	Asp	Gly	Gln	Glu	Leu 365	
_				_	att Ile					_	_		_			1212
_			_	_	aat Asn	_		_			_					1260
					cag Gln											1308
_	_	-	_		gtc Val	_		_	_		_			_		1356
				_	aaa Lys 435					-		_			_	1404
	_	_	_		gag Glu			_		-		-				1452
				_ ~	atc Ile	_	_				~			_		1500
		_	_		tcc Ser			-					_	_		1548
					aca Thr			_	_		_	-	-			1596
			_	-	ttt Phe 515											1644
					tgg Trp											1692
					cga Arg											1740
					ggt Gly											1788
_	_	_	_		aga Arg	_	_		-		_	_		-		1836
					agc Ser											1884

590					595					600					605		
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ctg Leu	aaa Lys	cgt Arg	ggt Gly 625	gat Asp	cag Gln	att Ile	atg Met	gaa Glu 630	gta Val	aat Asn	gga Gly	caa Gln	aac Asn 635	ttt Phe	gag Glu	1	980
aat Asn	att Ile	aca Thr 640	ttt Phe	atg Met	aaa Lys	gcc Ala	gtt Val 645	gaa Glu	att Ile	ttg Leu	agg Arg	aat Asn 650	aat Asn	act Thr	cat His	2	028
ctt Leu	gca Ala 655	ctt Leu	act Thr	gtg Val	aag Lys	acc Thr 660	aac Asn	att Ile	ttt Phe	gtg Val	ttc Phe 665	aaa Lys	gag Glu	tta Leu	ctt Leu	2	076
ttt Phe 670	agg Arg	act Thr	gaa Glu	caa Gln	gag Glu 675	aaa Lys	tct Ser	ggt Gly	gtt Val	cct Pro 680	cat His	att Ile	ccc Pro	aaa Lys	att Ile 685	2	124
gct Ala	gaa Glu	aaa Lys	aaa Lys	agt Ser 690	aat Asn	cgc Arg	cat His	tct Ser	atc Ile 695	cag Gln	cat His	gtg Val	cca Pro	gga Gly 700	gat Asp	2	172
att Ile	gaa Glu	cag Gln	aca Thr 705	tca Ser	cag Gln	gag Glu	aaa Lys	gga Gly 710	agt Ser	aag Lys	aaa Lys	gtt Val	aaa Lys 715	gca Ala	aat Asn	2:	220
act Thr	gtt Val	tca Ser 720	ggt Gly	gga Gly	aga Arg	aac Asn	aaa Lys 725	atc Ile	agg Arg	aag Lys	att Ile	ttg Leu 730	gat Asp	aaa Lys	aca Thr	2:	268
cga Arg	ttt Phe 735	agt Ser	atc Ile	ttg Leu	cct Pro	cca Pro 740	aag Lys	cta Leu	ttt Phe	agt Ser	gat Asp 745	gga Gly	ggc Gly	cta Leu	agc Ser	2:	316
caa Gln 750	tca Ser	caa Gln	gat Asp	gac Asp	agc Ser 755	att Ile	gtg Val	gga Gly	aca Thr	agg Arg 760	cac His	tgt Cys	agg Arg	cat His	agt Ser 765	2:	364
ctg Leu	gct Ala	ata Ile	atg Met	ccc Pro 770	atc Ile	cct Pro	gga Gly	aca Thr	ctc Leu 775	tca Ser	tcc Ser	agc Ser	agc Ser	cct Pro 780	gat Asp	24	412
ctc Leu	ctg Leu	cag Gln	cct Pro 785	acc Thr	acc Thr	agt Ser	atg Met	ttg Leu 790	gat Asp	ttt Phe	tcc Ser	aat Asn	cct Pro 795	tca Ser	gat Asp	24	460
atc Ile	cct Pro	gat Asp 800	caa Gln	gtt Val	ata Ile	aga Arg	gtt Val 805	ttc Phe	aaa Lys	gtg Val	gat Asp	cag Gln 810	caa Gln	agt Ser	tgc Cys	25	508
tac Tyr	att Ile 815	atc Ile	atc Ile	agt Ser	aaa Lys	gac Asp 820	acc Thr	aca Thr	gct Ala	aaa Lys	gaa Glu 825	gta Val	gtt Val	ttt Phe	cat His	25	556
gct Ala 830	gtt Val	cat His	gaa Glu	ttt Phe	ggt Gly 835	ttg Leu	acc Thr	ggt Gly	gca Ala	tcc Ser 840	gac Asp	aca Thr	tat Tyr	tct Ser	ctc Leu 845	26	504

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	aaa aat aac Lys Asn Asn		_		_
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_	att gaa ccg lle Glu Pro 930			_	Leu
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	aca ttc tgg Thr Phe Trp				
-	cga atg aag Arg Met Lys	_		_	
	gaa tgt aag Glu Cys Lys 995				
	ctg gca tct Leu Ala Ser 1010	Val Ala Arg			Lys
	e aaa tac gag Lys Tyr Glu 1025				
	aga aac atg Arg Asn Met		Arg Asn Ile		
	g cct cca att n Pro Pro Ile				
	cta cat gaa Leu His Glu 1075				

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cga Arg	atg Met	act Thr	tct Ser 1105	gct Ala	aac Asn	atg Met	Asp	cca Pro 1110	gct Ala	atg Met	atg Met	Phe	cga Arg 1115	cag Gln	agg Arg	3420
tca Ser	Leu	agt Ser 1120	caa Gln	gga Gly	agc Ser	Thr	aat Asn l125	tca Ser	aac Asn	atg Met	Leu	gat Asp 1130	gtt Val	cag Gln	gga Gly	3468
Gly	gct Ala 1135	cac His	aaa Lys	aaa Lys	Arg	gca Ala 1140	cgc Arg	cgc Arg	agc Ser	Ser	ctg Leu 1145	ctt Leu	aat Asn	gcc Ala	aag Lys	3516
Lys 1150	Leu	tat Tyr	Glu	Asp	Ala 1155	Gln	Met	Ala	Arg	Lys 1160	Val	Lys	Gln	Tyr	Leu 1165	3564
Ser	Ser	ctc Leu	Asp :	Val 1170	Glu	Thr	Asp	Glu :	Glu 1175	Lys	Phe	Gln	Met :	Met 1180	Ser	3612
Leu	Gln		Glu L185	Pro	Ala	Tyr	Gly 1	Thr 190	Leu	Thr	Lys	Asn 1	Leu 195	Ser	Glu	3660
Lys	Arg	tca Ser L200	Ala	Lys	Ser	Ser 1	Glu .205	Met	Ser	Pro	Val	Pro .210	Met	Arg	Ser	3708
Ala	Gly 1215	caa Gln	Thr	Thr	Lys 1	Ala .220	His	Leu	His	Gln	Pro 1225	His	Arg	Val	Ser	3756
Gln 1230	Val	ctt Leu	Gln	Val	Pro 1235	Ala	Val	Asn	Leu 1	His .240	Pro	Ile	Arg	Lys 1	Lys 1245	3804
Gly	Gln	aca Thr	Lys 1	Asp .250	Pro	Ala	Leu	Asn 1	Thr .255	Ser	Leu	Pro	Gln 1	Lys 1260	Val	3852
Leu	Gly		Thr .265	Glu	Glu	Ile	Ser 1	Gly 270	Lys	Lys	His	Thr 1	Glu 275	Asp	Thr	3900
Ile	Ser 1	gtg Val .280	Ala	Ser	Ser	Leu 1	His 285	Ser	Ser	Pro	Pro 1	Ala 290	Ser	Pro	Gln	3948
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Asn 1310	Leu	tct Ser	Asp	Ser 1	Ser .315	His	Ser	Glu	Ile 1	Ser 320	Ser	Arg	Ser	Ser 1	Ile 325	4044
gtg	agc	aat	tgt	tct	gtt	gac	tcc		tct	gca	gct	cta	cag	gat	gaa	4092

	Cys Ser 1330	Val Asp	Ser Met Ser 1335		u Gln Asp Glu 1340	
Arg Cys Ser	_			_	t ggg gca ttg r Gly Ala Leu 1355	
		Ala Ser		_	t caa cat ggc r Gln His Gly 0	
					t tta gct gtc s Leu Ala Val	
	Val Ser				t atc att ata s Ile Ile Ile 1405	
	_			Thr Ser Cys	t tca agc agc s Ser Ser Ser 1420	
Ser His Asp					c tgg gat ttt r Trp Asp Phe 1435	
_	_	His Thr		_	t gct gaa gtt e Ala Glu Val 0	
gaa ccc act	gac tct	gag ccc	tat tcc tgt	tct aaa ag	c tgc tct aga	4476
Glu Pro Thr 1455	Asp Ser	Glu Pro '	_	_	r Cys Ser Arg	
1455 act tgt ggg	cag tgt Gln Cys	1460 aaa gga	Tyr Ser Cys agc cta gag	Ser Lys Ser 1465 aga aag ag	-	4524
1455 act tgt ggg Thr Cys Gly 1470 tcc agt tct	cag tgt Gln Cys ctg tct	1460 aaa gga Lys Gly 1475 gac acg	Tyr Ser Cys agc cta gag Ser Leu Glu tat gaa cca	Ser Lys Ser 1465 aga aag agt Arg Lys Ser 1480 aac tat gg Asn Tyr Gl	r Cys Ser Arg t tgg acc tcc r Trp Thr Ser	4524
act tgt ggg Thr Cys Gly 1470 tcc agt tct Ser Ser Ser cgg aga gta Arg Arg Val	cag tgt Gln Cys ctg tct Leu Ser 1490 ttg gag	aaa gga Lys Gly 1475 gac acg Asp Thr	Tyr Ser Cys agc cta gag Ser Leu Glu tat gaa cca Tyr Glu Pro 1495 cca gct gag	Ser Lys Ser 1465 aga aag aga Arg Lys Ser 1480 aac tat gga Asn Tyr Gl	t tgg acc tcc r Trp Thr Ser 1485 g aca gtt aaa y Thr Val Lys	4524 4572 4620
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1570 1575 1580 tat agt gtg gca gtg cag agg tca aag atg atg cat aac agc ctc tct 4860 Tyr Ser Val Ala Val Gln Arg Ser Lys Met Met His Asn Ser Leu Ser 1585 1590 aga ctg cca cca gct tct ctc agt agc aac ctc gtg gcc tgt gtt cca 4908 Arg Leu Pro Pro Ala Ser Leu Ser Ser Asn Leu Val Ala Cys Val Pro 1605 1610 tcg aag att gta act cag cct cag agg cat aat ttg cag cca ttc cat 4956 Ser Lys Ile Val Thr Gln Pro Gln Arg His Asn Leu Gln Pro Phe His 1620 1625 cct aaa cta gga gat gtg act gat gca gat agc gaa gca gat gaa aat 5004 Pro Lys Leu Gly Asp Val Thr Asp Ala Asp Ser Glu Ala Asp Glu Asn 1630 1635 1640 gaa caa gtt tca gca gtc tag cc tttggatgac ctatttgaaa accactgaaa 5057 Glu Gln Val Ser Ala Val gtcgtggagg aatgggcaag aaccacctca tgattctgca ggccattgct aacgaacagc 5117 tcattgctac aaccagtcca gaggttttat tccctctact ccgagcaatg aaatagacct 5177 gagttatgct tcctttcatt taatttctgc agataaatag tttcctgagc aatggatgct 5237 atgeetggat accagtetee actttgeaeg eeggaaetge ettgggaeea cagttacaga 5297 aaaaatgtaa actcagagtg atccttgtgt atattgctat agatttttct ttaacaagct 5357 attttaaaga taatggcatt attatttcca agccatagct tgggctgaag gacaaattga 5417 aattgtctgc caataccaag gatattcttg tatatttgaa aaataactta ttatttgaat 5477 tgttgtggtt ttgtttgtat ttgagagete ttgttagetg atattcatgt ttgaggtcat 5537 aaaattgtct ctggtctgac caaacagaag tcatctttac agaggtgata tgcttgatct 5597 acacagagat gtgacttgat ctgtagcacc aatgcaatgt aggtctcagt ttgagagaaa 5657 taggaagece tttgeagttg aggtgttagg aacetgetgg teatggtgtg gaaggecaaa 5717 tgaagctgcc acagggtttc ttgtcagtcc tttgggaaat gggagggagt agtttgggga 5777 ggagggtggg aaccctaatt tccacagaat gaaattttga tgttaaatga catgtataca 5837 aattetteet taagtgaaag ttatgetgea tegaattgta aetgaaagta tagateeaae 5897 aaatagagac tgggttctag agagttctgg tctatagaaa cccaaaacta aaatctctca 5957 taactcaagt atggaatact ttttttaaag aaattcttat catgggtgtt gtaataatga 6017 agacgaattt gactttatgc agtgttttgc agcatgcctc ccccacatct catagcacca 6077 ggttgtgtct gacctgacat accctgcagc tctcagctgg ctgcagtaac attttgtggg 6137 agaaagagga gctggagtta cagaaatgat tgtctcttgg ttctcagttt ttagcccttg 6197 agaggacata cttttccagc ctcatgggta tggcactctt aattaaaatt tcagtgactg 6257

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148

484

Ser Val Gly Gln Ile Cys Thr Ala Pro Ala Glu Thr Ser His Pro Val

ctg ctg act gtg gag cag aga aag ctg tct tcc ctg tta gag ttt

Leu Leu Thr Val Glu Gln Arg Lys Lys Leu Ser Ser Leu Leu Glu Phe

gct cag tat tta ttg gca cac agt atg ttc tcc cgt ctt tcc tgt

125

140

120

Ala	Gln	Tyr	Leu 155	Leu	Ala	His	Ser	Met 160		Ser	Arg	Leu	Ser 165		сув	
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cat His	ctt Leu 185	His	gta Val	caa Gln	ggc	att Ile 190	gtg Val	agc Ser	ctg Leu	caa Gln	gag Glu 195	ctg Leu	ctg Leu	gaa Glu	agc Ser	628
cat His 200	Pro	gac Asp	atg Met	cat His	gct Ala 205	gtg Val	gga Gly	tcg Ser	tgg Trp	ctc Leu 210	ttc Phe	agg Arg	aat Asn	ctg Leu	tgc Cys 215	676
tgc Cys	ctt Leu	tgt Cys	gaa Glu	cag Gln 220	atg Met	gaa Glu	gca Ala	tcc Ser	tgc Cys 225	cag Gln	cat His	gct Ala	gac Asp	gtc Val 230	gcc Ala	724
Arg	Ala	Met	Leu 235	Ser	Asp	Phe	Val	Gln 240	Met	Phe	Val	ttg Leu	Arg 245	Gly	Phe	772
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Ala 280	Leu	Ala	Ala	Gly	Val 285	Gln	Glu	Glu	Ser	Ser 290	Thr	cac His	Lys	Ile	V al 295	916
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tcc Ser	aca Thr	gat Asp	cct Pro 315	ctg Leu	aag Lys	agg Arg	ttc Phe	ttc Phe 320	agt Ser	cat His	acc Thr	ctg Leu	act Thr 325	cag Gln	ata Ile	1012
Leu	Thr	His 330	Ser	Pro	Val	Leu	Lys 335	Ala	Ser	Asp	Ala	gtt Val 340	Gln	Met	Gln	1060
Arg	Glu 345	Trp	Ser	Phe	Ala	Arg 350	Thr	His	Pro	Leu	Leu 355	acc Thr	Ser	Leu	Tyr	1108
Arg 360	Arg	Leu	Phe	Val	Met 365	Leu	Ser	Ala	Glu	Glu 370	Leu	gtt Val	Gly	His	Leu 375	1156
Gln	Glu	Val	Leu	Glu 380	Thr	Gln	Glu	Val	His 385	Trp	Gln	aga Arg	Val	Leu 390	Ser	1204
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395 400 405 gaa gac tgg gtg gcg cgt ttg atg gcc cag gca ttc gag agc tgc cag 1300 Glu Asp Trp Val Ala Arg Leu Met Ala Gln Ala Phe Glu Ser Cys Gln 415 ctg gac agc atg gtc act gcg ttc ctg gtt gtg cgc cag gca gca ctg 1348 Leu Asp Ser Met Val Thr Ala Phe Leu Val Val Arg Gln Ala Ala Leu 430 gag ggc ccc tct gcg ttc ctg tca tat gca gac tgg ttc aag gcc tcc 1396 Glu Gly Pro Ser Ala Phe Leu Ser Tyr Ala Asp Trp Phe Lys Ala Ser ttt ggg agc aca cga ggc tac cat ggc tgc agc aag aag gcc ctg gtc 1444 Phe Gly Ser Thr Arg Gly Tyr His Gly Cys Ser Lys Lys Ala Leu Val 460 465 ttc ctg ttt acg ttc ttg tca gaa ctc gtg cct ttt gag tct ccc cgg 1492 Phe Leu Phe Thr Phe Leu Ser Glu Leu Val Pro Phe Glu Ser Pro Arg tac ctg cag gtg cac att ctc cac cca ccc ctg gtt ccc agc aag tac 1540 Tyr Leu Gln Val His Ile Leu His Pro Pro Leu Val Pro Ser Lys Tyr 495 cgc tcc ctc ctc aca gac tac atc tca ttg gcc aag aca cgg ctg gcc 1588 Arg Ser Leu Leu Thr Asp Tyr Ile Ser Leu Ala Lys Thr Arg Leu Ala 510 gac ctc aag gtt tct ata gaa aac atg gga ctc tac gag gat ttg tca 1636 Asp Leu Lys Val Ser Ile Glu Asn Met Gly Leu Tyr Glu Asp Leu Ser tca gct ggg gac att act gag ccc cac agc caa gct ctt cag gat gtt 1684 Ser Ala Gly Asp Ile Thr Glu Pro His Ser Gln Ala Leu Gln Asp Val 540 gaa aag gcc atc atg gtg ttt gag cat acg ggg aac atc cca gtc acc 1732 Glu Lys Ala Ile Met Val Phe Glu His Thr Gly Asn Ile Pro Val Thr 555 gtc atg gag gcc agc ata ttc agg agg cct tac tac gtg tcc cac ttc 1780 Val Met Glu Ala Ser Ile Phe Arg Arg Pro Tyr Tyr Val Ser His Phe 570 etc ecc gec etg etc aca ect ega gtg etc ecc aaa gte eet gae tec 1828 Leu Pro Ala Leu Leu Thr Pro Arg Val Leu Pro Lys Val Pro Asp Ser 585 cgt gtg gcg ttt ata gag tct ctg aag aga gca gat aaa atc ccc cca 1876 Arg Val Ala Phe Ile Glu Ser Leu Lys Arg Ala Asp Lys Ile Pro Pro 600 605 tct ctg tac tcc acc tac tgc cag gcc tgc tct gct gca gag aag 1924 Ser Leu Tyr Ser Thr Tyr Cys Gln Ala Cys Ser Ala Ala Glu Glu Lys 620 cca gaa gat gca gcc ctg gga gtg agg gca gaa ccc aac tct gct gag 1972 Pro Glu Asp Ala Ala Leu Gly Val Arg Ala Glu Pro Asn Ser Ala Glu

635

gag Glu	ccc Pro	ctg Leu 650	gga Gly	cag Gln	ctc Leu	aca Thr	gct Ala 655	gca Ala	ctg Leu	gga Gly	gag Glu	ctg Leu 660	aga Arg	gcc Ala	tcc Ser	2020
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														gag Glu		•	2788
														cac His		2	2836
														gaa Glu 950		;	2884
cag Gln	gac Asp	ttc Phe	cac His 955	cag Gln	tgg Trp	gcg Ala	atc Ile	cat His 960	gag Glu	cac His	ttt Phe	ctc Leu	cct Pro 965	gag Glu	tcc Ser	2	2932
					_	_		_	_	-	_		_	acc Thr			2980
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				Ser					Gly					aat Asn		;	3076
_			Ser	_	_	_		Met	_	_	_	_	Glu	ctg Leu 1030	_	:	3124
		Leu					Gly					Gln		cac His		3	3172
Leu	Phe J	Glu 1050	Ile	Phe	Arg	Arg	Arg .055	Leu	Gln	Ala	Leu 1	Thr 1060	Ser	gly aaa	Trp	3	3220
Ser					Leu					Glu				tac Tyr		3	3268
				Arg					Val					agc Ser		;	3316
Gln	Ala	Glu	Gln	Pro 1100	Ile	Thr	Ala	Arg	Cys 1105	Glu	Gln	Phe	Phe	cac His L110	Leu	:	3364
		Ser					Phe					${\tt Gly}$		ctg Leu		:	3412
cag	gac	atc	act	gcc	cac	ttc	ttc	agg	ggc	ctc	ctg	aac	gcc	tgt	ctg	:	3460

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cgg agc aga Arg Ser Arg 1145	gac ccc tcc Asp Pro Ser	ctg atg gtc Leu Met Val 1150	gac ttc ata Asp Phe Ile 1155	ctg gcc aag Leu Ala Lys	tgc 3508 Cys
		Ile Leu Thr	tct gct ctg Ser Ala Leu 1170	Val Trp Trp	
agc ctg gag Ser Leu Glu	cct gtg ctg Pro Val Leu 1180	ctc tgc cgg Leu Cys Arg	tgg agg aga Trp Arg Arg 1185	cac tgc cag His Cys Gln 1190	agc 3604 Ser
Pro Leu Pro	cgg gaa ctg Arg Glu Leu 1195	cag aag cta Gln Lys Leu 1200	caa gaa ggc Gln Glu Gly	cgg cag ttt Arg Gln Phe 1205	gcc 3652 Ala
			tcc cca gca Ser Pro Ala 1		
tgg ctc tca Trp Leu Ser 1225	gct gct gca Ala Ala Ala	ctg cac ttt Leu His Phe 1230	gcg att caa Ala Ile Gln 1235	caa gtc agg Gln Val Arg	gaa 3748 Glu
		Leu Lys Lys	ctg gac tgc Leu Asp Cys 1250	Glu Arg Glu	
			ttg atg ggc Leu Met Gly 1265		
His Leu Thr			ctg cca aag Leu Pro Lys		
tgt gca gca Cys Ala Ala 1290	atc ctc gag Ile Leu Glu	tgt tta gag Cys Leu Glu 1295	aag agg aag Lys Arg Lys 1	ata tcc tgg Ile Ser Trp 300	ctg 3940 Leu
gca ctc ttt Ala Leu Phe 1305	Gln Leu Thr	gag agt gac Glu Ser Asp 1310	ctc agg ctg Leu Arg Leu 1315	ggg cgg ctc Gly Arg Leu	ctc 3988 Leu
ctc cgt gtg Leu Arg Val 1320	gcc ccg gat Ala Pro Asp 1325	cag cac acc Gln His Thr	agg ctg ctg Arg Leu Leu 1330	Pro Phe Ala	ttt 4036 Phe 335
tac agt ctt Tyr Ser Leu	ctc tcc tac Leu Ser Tyr 1340	Phe His Glu	gac gcg gcc Asp Ala Ala 1345	atc agg gaa Ile Arg Glu 1350	gag 4084 Glu
Ala Phe Leu	cat gtt gct His Val Ala 1355	gtg gac atg Val Asp Met 1360	tac ttg aag Tyr Leu Lys	ctg gtc cag Leu Val Gln : 1365	ctc 4132 Leu
ttc gtg gct Phe Val Ala	ggg gat aca Gly Asp Thr	agc aca gtt Ser Thr Val	tca cct cca Ser Pro Pro	gct ggc agg a Ala Gly Arg	agc 4180 Ser

1380

1375

ctg gag ctc aag ggt cag gca ggg caa ccc cgt gga act gat aac aaa 4228 Leu Glu Leu Lys Gly Gln Ala Gly Gln Pro Arg Gly Thr Asp Asn Lys 1385 1390 age teg tet ttt tet get gea gtt aat ace teg gtg eee gaa aaa gag 4276 Ser Ser Ser Phe Ser Ala Ala Val Asn Thr Ser Val Pro Glu Lys Glu 1400 1405 1410 1415 ctt ctc aca cgt ggc aga gct gct ggc tga t cgtggggact gcgacccaga 4327 Leu Leu Thr Arg Gly Arg Ala Ala Gly 1420 ggtgagcgcc gccctccaga gcagacagca ggctgcccct gacgctgacc tgtcccagga 4387 gcctcatctc ttctgacggg acctgccact gcacaccagc ccagctcccg tgtaaataat 4447 ttattacaag cataacatgg agetettgtt gcactaaaaa gtggattaca aateteeteg 4507 actgctttag tggggaaagg aatcaattat ttatgaactg tccggccccg agtcactcag 4567 cgtttgcggg aaaataaacc actggtccca gagcagagga aggctacttg agccggacac 4627 caagcccgcc tccagcacca agggcgggca gcaccctccg accctcccat gcgggtgcac 4687 acgaagggtg aggetgacae agecaetgeg gagteeagge tgetagaggt geteateete 4747 actgccgtcc tcaggtgggt tcgggcttca ccgcctggcc ctctgtggtc acagaggggc 4807 teggtggecc aggtggtggt teegeeteea ggggeaggge ettgteetgg gtetgtgtea 4867 gcgggtgcac catggacatg tgtacattga ggttgtgggc cttctcaaac cgccggccac 4927 actggtcaca ggcaaagtcc agctcagtct cagccttgtg tttggtcatg tggtacttga 4987 gggatgcccg ctgcctgcac tggaacccac agacctcaca cctgggggac agaggcagat 5047 aagaaggtgc gagggccaca gccctgggag ggggtcctga ctcacactta ctgcaaaggc 5107 ttggctcccg aatgtcgcat ttggtggacg agaaggtgct tccgctgctt gaaggtttgt 5167 ccacattcgt cacagatata gttccgcacc tctgagaggg gagagtccag tgagtccagg 5227 cccctgatgc tccaacctcc cggggggacg acgatgacaa tgtgaaacca tcacagctgg 5287 gaagacattt ctgcacatgg ttcaccatgc agtgggccca agcaaggggc ctatgagggc 5347 ctcgtttatt aagatcttta aactgcttta tacactgtca cgtggcttca tcagctgtgt 5407 gcatttcagg atggttttta aagaaacctc agaaagctat ttccttaaaa aaaaaaaa 5466

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tgc ctt tgt gaa cag atg gaa gca tcc tgc cag cat gct gac gtc gcc

205

200

Cys	Leu	Сув	Glu	Gln 220	Met	Glu	Ala	Ser	Cys 225	Gln	His	Ala	Asp	Val 230	Ala	
	gcc Ala															772
_	aaa Lys			_	_	_	_			-						820
	gtc Val 265															868
	ttg Leu															916
	tgc Cys															964
	aca Thr	_		_	_				_			-		_		1012
	act Thr															1060
	gag Glu 345															1108
	agg Arg															1156
	gaa Glu															1204
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gaa Glu	gac Asp	tgg Trp 410	gtg Val	gcg Ala	cgt Arg	ttg Leu	atg Met 415	gcc Ala	cag Gln	gca Ala	ttc Phe	gag Glu 420	agc Ser	tgc Cys	cag Gln	1300
	gac Asp 425															1348
gag Glu 440	Gly	ccc Pro	tct Ser	gcg Ala	ttc Phe 445	ctg Leu	tca Ser	tat Tyr	gca Ala	gac Asp 450	tgg Trp	ttc Phe	aag Lys	gcc Ala	tcc Ser 455	1396
ttt Phe	Gly Gly	agc Ser	aca Thr	cga Arg	ggc Gly	tac Tyr	cat His	ggc	tgc Cys	agc Ser	aag Lys	aag Lys	gcc Ala	ctg Leu	gtc Val	1444

				460					465					470			
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tac Tyr	ctg Leu	cag Gln 490	gtg Val	cac His	att Ile	ctc Leu	cac His 495	cca Pro	ccc Pro	ctg Leu	gtt Val	ccc Pro 500	agc Ser	aag Lys	tac Tyr		1540
cgc Arg	tcc Ser 505	ctc Leu	ctc Leu	aca Thr	gac Asp	tac Tyr 510	atc Ile	tca Ser	ttg Leu	gcc Ala	aag Lys 515	aca Thr	cgg Arg	ctg Leu	gcc Ala		1588
gac Asp 520	ctc Leu	aag Lys	gtt Val	tct Ser	ata Ile 525	gaa Glu	aac Asn	atg Met	gga Gly	ctc Leu 530	tac Tyr	gag Glu	gat Asp	ttg Leu	tca Ser 535		1636
tca Ser	gct Ala	Gly 999	gac Asp	att Ile 540	act Thr	gag Glu	ccc Pro	cac His	agc Ser 545	caa Gln	gct Ala	ctt Leu	cag Gln	gat Asp 550	gtt Val		1684
gaa Glu	aag Lys	gcc Ala	atc Ile 555	atg Met	gtg Val	ttt Phe	gag Glu	cat His 560	acg Thr	gjå aaa	aac Asn	atc Ile	cca Pro 565	gtc Val	acc Thr	:	1732
gtc Val	atg Met	gag Glu 570	gcc Ala	agc Ser	ata Ile	ttc Phe	agg Arg 575	agg Arg	cct Pro	tac Tyr	tac Tyr	gtg Val 580	tcc Ser	cac His	ttc Phe	;	1780
ctc Leu	ccc Pro 585	gcc Ala	ctg Leu	ctc Leu	aca Thr	cct Pro 590	cga Arg	gtg Val	ctc Leu	ccc Pro	aaa Lys 595	gtc Val	cct Pro	gac Asp	tcc Ser	;	1828
cgt Arg 600	gtg Val	gcg Ala	ttt Phe	ata Ile	gag Glu 605	tct Ser	ctg Leu	aag Lys	aga Arg	gca Ala 610	gat Asp	aaa Lys	atc Ile	ccc Pro	cca Pro 615	;	1876
tct Ser	ctg Leu	tac Tyr	tcc Ser	acc Thr 620	tac Tyr	tgc Cys	cag Gln	gcc Ala	tgc Cys 625	tct Ser	gct Ala	gct Ala	gaa Glu	gag Glu 630	aag Lys	;	1924
cca Pro	gaa Glu	gat Asp	gca Ala 635	gcc Ala	ctg Leu	gga Gly	gtg Val	agg Arg 640	gca Ala	gaa Glu	ccc Pro	aac Asn	tct Ser 645	gct Ala	gag Glu	:	1972
gag Glu	ccc Pro	ctg Leu 650	gga Gly	cag Gln	ctc Leu	aca Thr	gct Ala 655	gca Ala	ctg Leu	gga Gly	gag Glu	ctg Leu 660	aga Arg	gcc Ala	tcc Ser	:	2020
atg Met	aca Thr 665	gac Asp	ccc Pro	agc Ser	cag Gln	cgt Arg 670	gat Asp	gtt Val	ata Ile	tcg Ser	gca Ala 675	cag Gln	gtg Val	gca Ala	gtg Val	:	2068
att Ile 680	tct Ser	gaa Glu	aga Arg	ctg Leu	agg Arg 685	gct Ala	gtc Val	ctg Leu	ggc Gly	cac His 690	aat Asn	gag Glu	gat Asp	gac Asp	agc Ser 695	;	2116
agc Ser	gtt Val	gag Glu	ata Ile	tca Ser 700	aag Lys	att Ile	cag Gln	ctc Leu	agc Ser 705	atc Ile	aac Asn	acg Thr	ccg Pro	aga Arg 710	ctg Leu	2	2164

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	ctg Leu 730														.2260
	gct Ala														2308
	ctc Leu				_	-	_		_		_		_	-	2356
	gcc Ala														2404
	tcc Ser														2452
	gct Ala 810														2500
_	 acg Thr		_		_			_	_			_		_	2548
_	tct Ser				_	_				_		_	_		2596
_	agc Ser	-								_		_			2644
	aga Arg														2692
	agc Ser 890														2740
	gct Ala														2788
_	gag Glu	-	_	_						_				_	2836
_	gaa Glu				_	_	_	-			_		_		2884

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	aca Thr															2980
	ctg Leu 985															3028
	cag Gln			Phe					Phe					Gln		3076
	aca Thr		Gly					Āla					Gln			3124
	cta Leu	Met					Leu					Ser				3172
	ggc Gly		-		_	Āla		_			Thr	_	_	_		3220
Gln	ttc Phe 1065			_	Val				_	Arg						3268
	ggt Gly		_	Thr	_	_			Āla					Gly		3316
	aac Asn		Cys					Asp					Val			3364
	ctg Leu	Ala					Lys					Leu				3412
ctg Leu	gtg Val	tgg Trp L130	tgg Trp	ccg Pro	agc Ser	Leu	gag Glu 135	cct Pro	gtg Val	ctg Leu	Leu	tgc Cys 140	cgg Arg	tgg Trp	agg Arg	3460
aga Arg	Cac	taa	C2C	200		ata							-4-		~~~	3508
-	His 1145	Сув	Gln	Ser	Pro	Leu 150	Pro	Arg	Glu	Leu	Cag Gln 155	Lys	Leu	Gln	Glu	
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ggc Gly 1160 gca	His 1145 cgg	Cys cag Gln aac	ttt Phe ccg Pro	gcc Ala gac	agc Ser 1165	Leu 150 gat Asp	Pro ttc Phe tca	ctc Leu gct Ala	Glu tcc Ser gct	cct Pro 170	Gln 155 gag Glu ctg	Lys gct Ala cac	gcc Ala ttt Phe	Gln tcc Ser J	CCa Pro 175	

Gln Gln Val Arg Glu Glu Asn Ile Arg Lys Gln Leu Lys Lys Leu Asp 1200 tgc gag aga gag gag cta ttg gtt ttc ctt ttc ttc tcc ttg atg 3700 Cys Glu Arg Glu Glu Leu Leu Val Phe Leu Phe Phe Phe Ser Leu Met 1210 1215 ggc ctg ctg tcg tca cat ctg acc tca aat agc acc aca gac ctg cca 3748 Gly Leu Leu Ser Ser His Leu Thr Ser Asn Ser Thr Thr Asp Leu Pro 1225 aag gct ttc cac gtt tgt gca gca atc ctc gag tgt tta gag aag agg 3796 Lys Ala Phe His Val Cys Ala Ala Ile Leu Glu Cys Leu Glu Lys Arg 1240 1245 1250 aag ata tcc tgg ctg gca ctc ttt cag ttg aca gag agt gac ctc agg 3844 Lys Ile Ser Trp Leu Ala Leu Phe Gln Leu Thr Glu Ser Asp Leu Arg 1260 1270 ctg ggg cgg ctc ctc ctc cgt gtg gcc ccg gat cag cac acc agg ctg 3892 Leu Gly Arg Leu Leu Arg Val Ala Pro Asp Gln His Thr Arg Leu 1275 1280 ctg cct ttc gct ttt tac agt ctt ctc tcc tac ttc cat gaa gac gcg 3940 Leu Pro Phe Ala Phe Tyr Ser Leu Leu Ser Tyr Phe His Glu Asp Ala 1290 1295 gcc atc agg gaa gag gcc ttc ctg cat gtt gct gtg gac atg tac ttg 3988 Ala Ile Arg Glu Glu Ala Phe Leu His Val Ala Val Asp Met Tyr Leu 1315 aag ctg gtc cag ctc ttc gtg gct ggg gat aca agc aca gtt tca cct 4036 Lys Leu Val Gln Leu Phe Val Ala Gly Asp Thr Ser Thr Val Ser Pro 1320 1325 cca gct ggc agg agc ctg gag ctc aag ggt cag gca ggg caa ccc cgt 4084 Pro Ala Gly Arg Ser Leu Glu Leu Lys Gly Gln Ala Gly Gln Pro Arg 1340 1345 gga act gat aac aaa agc tcg tct ttt tct gct gca gtt aat acc tcg 4132 Gly Thr Asp Asn Lys Ser Ser Ser Phe Ser Ala Ala Val Asn Thr Ser 1360 gtg ccc gaa aaa gag ctt ctc aca cgt ggc aga gct gct ggc tga tcg 4180 Val Pro Glu Lys Glu Leu Leu Thr Arg Gly Arg Ala Ala Gly 1375 tggggactgc gacccagagg tgagcgccgc cctccagagc agacagcagg ctgccctga 4240 egetgaeetg teecaggage eteatetett etgaegggae etgecaetge acaeeageee 4300 agctcccgtg taaataattt attacaagca taacatggag ctcttgttgc actaaaaagt 4360 ggattacaaa tctcctcgac tgctttagtg gggaaaggaa tcaattattt atgaactgtc 4420 cggccccgag tcactcagcg tttgcgggaa aataaaccac tggtcccaga gcagaggaag 4480 gctacttgag ccggacacca agcccgcctc cagcaccaag ggcgggcagc accctccgac 4540 cctcccatge gggtgcacac gaagggtgag gctgacacag ccactgcgga gtccaggctg 4600

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age eta etg ege ett gge ege ggg eta aca gte ege tge gge eee ggg Ser Leu Leu Arg Leu Gly Arg Gly Leu Thr Val Arg Cys Gly Pro Gly

221

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caa ggt cac ggg gag att cac cga gtc ccc acg cag cgc agg cct tcg 365 Gln Gly His Gly Glu Ile His Arg Val Pro Thr Gln Arg Arg Pro Ser

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														tcg Ser 85		413
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		Ala	Arg				_			_				aca Thr		509
														gaa Glu		557
														tgg Trp		605
			gca Ala									tga	tat	tctaa	agt	654
gaca	aagt	gt t	cac	ctgaa	at a	ccato	cccts	g tca	atcag	gcaa	cag	taga	aga 1	tggga	aaaaat	714
agaa	tatt	ta d	ccaa	aatai	c to	gccat	ggtt	tta	attti	ggt	aaca	aagaa	agc a	acaat	gtctt	774
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gtga	agat	gt a	agaat	tatte	gg ca	acac	cttca	a cag	geet	catt	cct	geeti	ttt (ctcag	gccatt	954
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aac tgg gca atc cat aca gga aag cat caa cca gga gta gat aaa cct Asn Trp Ala Ile His Thr Gly Lys His Gln Pro Gly Val Asp Lys Pro 20 25 30	631
gat ccc aaa aca tgg aag gcg aat ttc aga tgc gcc atg aat tcc ttg Asp Pro Lys Thr Trp Lys Ala Asn Phe Arg Cys Ala Met Asn Ser Leu 35 40 45 50	679
cct gat att gaa gaa gtc aag gat aaa agc ata aag aaa gga aat aat Pro Asp Ile Glu Glu Val Lys Asp Lys Ser Ile Lys Lys Gly Asn Asn 55 60 65	727
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gat ctt tct cct gag tat gcg gtc ctg act tca act ata aaa aat gaa Asp Leu Ser Pro Glu Tyr Ala Val Leu Thr Ser Thr Ile Lys Asn Glu 115 120 125 130	919
gtg gat agt acg gtg aac atc ata gtt gta gga cag tcc cat ctg gac Val Asp Ser Thr Val Asn Ile Ile Val Val Gly Gln Ser His Leu Asp 135 140	967
agc aac att gag aat caa gag att gtc acc aat ccg cca gac att tgc Ser Asn Ile Glu Asn Gln Glu Ile Val Thr Asn Pro Pro Asp Ile Cys 150 155 160	1015
caa gtt gta gag gtg acc act gag agc gac gag cag ccg gtc agc atg Gln Val Val Glu Val Thr Thr Glu Ser Asp Glu Gln Pro Val Ser Met 165 170 175	1063
age gag ete tae eet etg eag ate tee eec gtg tet tee tat gea gaa Ser Glu Leu Tyr Pro Leu Gln Ile Ser Pro Val Ser Ser Tyr Ala Glu 180 185 190	1111
agc gaa acg act gat agt gtg ccc agc gat gaa gag agt gcc gag gga	1159

Ser Gl	u Thr	Thr	Asp	Ser 200	Val	Pro	Ser	Asp	Glu 205	Glu	Ser	Ala	Glu	Gly 210	
cgg cca Arg Pro	a cac o His	tgg Trp	cgg Arg 215	aag Lys	agg Arg	aat Asn	att Ile	gaa Glu 220	ggc	aaa Lys	cag Gln	tac Tyr	çtc Leu 225	agc Ser	1207
aac atg Asn Me															1255
gtc act		Asn													1303
aat cc; Asn Pro	o Val														1351
ctt tci Leu Sei 275															1399
gag aco Glu Th		_	_	_		_	Lys		_	_			_	•	1447
cgc gte Arg Va				taa	gcct	ct g	gacto	eteeg	ac ac	gtggt	tgtt	999	ggctt	ctt	1501
ggcttt	gttt	tgtt	gtttg	ıt tt	gtat	ttta	ttt	tttt	ctc	tcts	gacac	ect a	atttt	agaca	1561
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agtctg	ette	tgca	cctta	t ct	taaa	agcac	: tta	acaga	atag	gcct	tctt	gt	gatct	tgctc	1921
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catccca	atcc	catco	ccato	C Ca	atcco	catco	cat	cccg	gctc	tttt	ccta	ict 1	tttco	etteec	2041
tcaaag	cttc	catt	ccaca	t co	ggag	ggaga	aga	agga	aat	gaat	ttct	ct a	acaga	tgtcc	2101
catttt	caga	ctgc	tttaa	a aa	aaaat	cctt	cta	atct	gct	atgo	ttga	at g	gccac	geggt	2161
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agattc	ettt	tctt	gttta	it ca	agcag	gttgt	tat	taca	tcc	ttgt	ggca	ica t	tttt	tttta	2401

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agg Arg	gtc Val	tac Tyr 25	cga Arg	atg Met	ctg Leu	ccc Pro	cta Leu 30	tca Ser	gaa Glu	cgg Arg	cct Pro	tct Ser 35	aag Lys	aaa Lys	gtt Val	15	i (
gta Val	gga Gly 40	cag Gln	tcc Ser	cat His	ctg Leu	gac Asp 45	agc Ser	aac Asn	att Ile	gag Glu	aat Asn 50	Caa Gln	gag Glu	att Ile	gtc Val	19	9 (
acc Thr 55	aat Asn	ccg Pro	cca Pro	gac Asp	att Ile 60	tgc Cys	caa Gln	gtt Val	gta Val	gag Glu 65	gtg Val	acc Thr	act Thr	gag Glu	agc Ser 70	24	. 6
gac Asp	gag Glu	cag Gln	ccg Pro	gtc Val 75	agc Ser	atg Met	agc Ser	gag Glu	ctc 80	tac Tyr	cct Pro	ctg Leu	cag Gln	atc Ile 85	tcc Ser	29	4
ccc Pro	gtg Val	tct Ser	tcc Ser 90	tat Tyr	gca Ala	gaa Glu	agc Ser	gaa Glu 95	acg Thr	act Thr	gat Asp	agt Ser	gtg Val 100	ccc Pro	agc Ser	34	.2
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gaa Glu	ggc Gly 120	Lys	Gln	tac Tyr	Leu	Ser	Asn	Met	Gly	Thr	cga Arg 130	Gly	tcc Ser	tac Tyr	ctg Leu	43	8
ctg Leu 135	ccc Pro	ggc Gly	atg Met	gcg Ala	tcc Ser 140	ttc Phe	gtc Val	act Thr	tcc Ser	aac Asn 145	aaa Lys	ccg Pro	gac Asp	ctc Leu	cag Gln 150	48	6
gtc Val	acc Thr	atc Ile	aaa Lys	gag Glu 155	gag Glu	agc Ser	aat Asn	ccg Pro	gtg Val 160	cct Pro	tac Tyr	aac Asn	agc Ser	tcc Ser 165	tgg Trp	53	4
ccc Pro	cct Pro	ttt Phe	caa Gln	gac Asp	ctc Leu	ccc Pro	ctt Leu	tct Ser	tcc Ser	tcc Ser	atg Met	acc Thr	cca	gca Ala	tcc	58	2

180

agc agc agt cgg cca g Ser Ser Ser Arg Pro A 185	ac cgt gag sp Arg Glu 190	acc cgg gcc Thr Arg Ala	agc gtc atc aag aaa Ser Val Ile Lys Lys 195	630
aca tcg gat atc acc co Thr Ser Asp Ile Thr G 200	ag gcc cgc ln Ala Arg 205	gtc aag agc Val Lys Ser	tgt taa gcctctgact Cys 210	679
ctccgcggtg gttgttgggg	cttcttggct	ttgttttgtt	gtttgtttgt attttatttt	739
tttctctctg acacctattt	tagacaaatc	taagggaaaa	agccttgaca atagaacatt	799
gattgctgtg tccaactcca	gtacctggag	cttctcttta	actcaggact ccagcccatt	859
ggtagacgtg tgtttctaga	gcctgctgga	tctcccaggg	ctactcactc aagttcaagg	919
accaacaagg gcagtggagg	tgctgcattg	cctgcggtca	aggccagcaa ggtggagtgg	979
atgcctcaga acggacgaga	taatgtgaac	tagctggaat	tttttattct tgtgaatatg	1039
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ccattcccca gcctctcttc	ctatcccatc	ccatcccatc	ccatcccatc ccatcccatc	1219
ccgctctttt cctacttttc	cttccctcaa	agcttccatt	ccacatccgg aggagaagaa	1279
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170

<213> Homo sapiens

<220> <221> CDS

<222> (66)..(1655)

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tct Ser 15	gcc Ala	act Thr	cca Pro	cag Gln	ggc Gly 20	agc Ser	agc Ser	agc Ser	tcg Ser	gac Asp 25	tct Ser	ctg Leu	gag Glu	ggc Gly	cag Gln 30	15	55
agc Ser	tgc Cys	gac Asp	tat Tyr	gcc Ala 35	agc Ser	aag Lys	agc Ser	tat Tyr	gat Asp 40	gcc Ala	gtt Val	gtc Val	ttc Phe	gat Asp 45	gtc Val	20)3
		gtg Val														25	51
		gtg Val 65														29	₹9
		aag Lys														34	į 7
acc Thr 95	cgg Arg	agg Arg	ttt Phe	aac Asn	cag Gln 100	gtc Val	agt Ser	ttt Phe	tgg Trp	gtt Val 105	gta Val	cga Arg	gaa Glu	att Ile	cta Leu 110	39	₹5
		cag Gln														44	13
		gcc Ala					_								_	45	1
		gta Val 145														53	19
		gct Ala				_		_	_						_	58	37
		ctg Leu														63	15
atc Ile	cga Arg	agc Ser	ctg Leu	aag Lys 195	atg Met	gtt Val	cca Pro	agt Ser	att Ile 200	ccc Pro	tat Tyr	cta Leu	gga Gly	atc Ile 205	tat Tyr	68	33
		gạt Asp														73	31
		gaa Glu 225														77	19
ata Ile	att Ile 240	gct Ala	gat Asp	tta Leu	Gln	gtt Val 245	tcc Ser	tgc Cys	agc Ser	tat Tyr	gat Asp	cac His	ctc Leu	acc Thr	acc Thr	82	! 7

ctg Leu 255	ccc Pro	cat His	gtg Val	cag Gln	aag Lys 260	tac Tyr	ctg Leu	aag Lys	tcc Ser	gta Val 265	cgc Arg	tac Tyr	att Ile	gaa Glu	gag Glu 270	875
ctc Leu	cag Gln	aag Lys	ttt Phe	gtg Val 275	gaa Glu	gac Asp	gac Asp	aac Asn	tac Tyr 280	aaa Lys	ctg Leu	tcg Ser	ctc Leu	aga Arg 285	atc Ile	923
		gga Gly		_			_					-	_	_		971
gca Ala	ggt Gly	ccc Pro 305	tct Ser	gct Ala	ggc Gly	tcc Ser	ggt Gly 310	tct Ser	gcg Ala	agg Arg	ttc Phe	agc Ser 315	cgg Arg	agg Arg	ccc Pro	1019
acc Thr	tgt Cys 320	cct Pro	gac Asp	aca Thr	tct Ser	gtt Val 325	gct Ala	ggc gly	agc Ser	ctc Leu	ccc Pro 330	aca Thr	cct Pro	cca Pro	gtc Val	1067
		cac His														1115
		acc Thr	_						_		_					1163
		cgg Arg		_	_		_				_	_		_		1211
ctg Leu	gly aaa	aac Asn 385	tcc Ser	gca Ala	gct Ala	gtg Val	ccc Pro 390	acc Thr	atg Met	gag Glu	gly aaa	cct Pro 395	ctg Leu	aga Arg	aga Arg	1259
		ctg Leu														1307
		tgg Trp														1355
		ttg Leu														1403
atg Met	gtg Val	cag Gln	ctg Leu 450	ccc Pro	gat Asp	gac Asp	ccc Pro	gag Glu 455	cac His	cca Pro	gat Asp	atc Ile	ttc Phe 460	cag Gln	ctg Leu	1451
		cct Pro 465														1499
ttt Phe	cat His 480	gca Ala	ata Ile	ctg Leu	tgg Trp	cac His 485	aag Lys	cat His	ttg Leu	gat Asp	gat Asp 490	gca Ala	tgt Cys	aaa Lys	agc Ser	1547

aac agg cet cag gaa gee gga gea get eea ggt eea aca gga aet gae Asn Arg Pro Gln Glu Ala Gly Ala Ala Pro Gly Pro Thr Gly Thr Asp 495 500 505 510	1595
agc cac gag gtg gac cac ctg gag ggc ggt gcg ggg aag gag gca ggg Ser His.Glu Val Asp His Leu Glu Gly Gly Ala Gly Lys Glu Ala Gly 515 520 525	1643
ccc tgt gcc tga agc ctgggcacca tggtggcccc agtcaggagc aacagtggta Pro Cys Ala	1698
gccctgagta aaacccattg tccctctttg gaggagcggc cagaggatga cagcagcccc	1758
agcaggcagc agtgcctggg caggctgatc cagcagagca ctaatgggtc agtttcatgt	1818
attggcagat gtggtgtagc atggcaaggc tacaagtttt aaggattttt gtctgatttt	1878
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tcaaccaaat attcccacta tgtgctatat gtaataataa aaagttgaca acaactgaaa	.1998
tattcaacag cagaggatga tttaagtgaa tcacagtaca tccgtgtgat ggaatgccag	2058
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cca ggg aca gag gcc agc gcg ctg caa cac aag atc aag aac tcc atc 258

cca ggg aca gag gcc agc gcg ctg caa cac aag atc aag aac tcc atc

Pro Gly Thr Glu Ala Ser Ala Leu Gln His Lys Ile Lys Asn Ser Ile

40

45

50

tgc aaa act gta caa tct aaa gtg gac tgc att ttg caa gaa gtt gag 306 Cys Lys Thr Val Gln Ser Lys Val Asp Cys Ile Leu Gln Glu Val Glu 55 60 65

	Phe		gac Asp													354
			aat Asn													402
			caa Gln 105													450
			gag Glu													498
			tgt Cys	_								_	_	_	_	546
			atc Ile	_			_				_	_	_	_	_	594
ttg Leu	ggc Gly	aca Thr	aga Arg	ggc Gly 170	aaa Lys	tct Ser	aaa Lys	tat Tyr	tgc Cys 175	tac Tyr	agt Ser	gga Gly	cta Leu	aga Arg 180	aaa Lys	642
			gtt Val 185		_			_				-				690
			GJA aaa	_	_		_	_				_				738
	_	_	gaa Glu	_				_	_	_			_			786
_	_		gtg Val		_				_		_	-	_			834
			gta Val													882
			atg Met 265													930
			ttt Phe													978
			ttg Leu													1026
aaa	atc	cag	aag	aag	cag	caa	gaa	cag	aaa	cta	caa	tcc	cct	ttg	cca	1074

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                                                                     1122
Gly Glu Ser Ala Ala Lys Lys Ser Glu Ser Ala Thr Ser Asn Gly Val
                330
                                    335
act aat ctt cct aat gga aat cct tca atc ctt tct cct caa cct att
                                                                     1170
Thr Asn Leu Pro Asn Gly Asn Pro Ser Ile Leu Ser Pro Gln Pro Ile
ggt atc gtt atg gca gct gtc cct agt ccc att ccg gtc cag cgg act
                                                                     1218
Gly Ile Val Met Ala Ala Val Pro Ser Pro Ile Pro Val Gln Arg Thr
agg cat ttg gta act tca ccg agt cca atg agt tct tct gac ggc aaa
                                                                     1266
Arg His Leu Val Thr Ser Pro Ser Pro Met Ser Ser Ser Asp Gly Lys
    375
gtt ctt ccc ctc aat gta cag gtg tca ctc agc aca tgc agt ctg tga
                                                                     1314
Val Leu Pro Leu Asn Val Gln Val Ser Leu Ser Thr Cys Ser Leu
390
                    395
aacaggcacc aaagactccc cagaacgttc cagccagtcc tggtggggat cgttctgccc
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ggcaccgtta ccctcagatc ttacccaaac cagcgaacac cagtgcactc accattcqct
                                                                     1434
ctccaactac tgtcctcttt actagtagtc ccatcaaaac tgctgttgta cccgcttcac
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                                                                     1794
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                                                                     1854
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                                                                     1914
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                                                                     1974
gtctgctagc at
                                                                     1986
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<222> (135)..(608)
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ttccttccgg agcc	_			tt gat ata ta le Asp Ile Ty 10	_						
gac gag gag ttc Asp Glu Glu Phe 15											
gac ctg tat gat Asp Leu Tyr Asp 30		Thr Ala 1		n Pro Ser Asp	_						
aga agc agc Arg Ser Ser Ser 45	_										
ccc aag ccc aac Pro Lys Pro Asn	_	-	_	_							
ctg cgt aat aga Leu Arg Asn Arg 80	Arg Ala Ala	_									
acc aca gac cag Thr Thr Asp Gln 95											
gat gtg gtg gag Asp Val Val Glu 110	-	Ala Glu A		a Asn Gly Gln							
aaa ggg tat gct Lys Gly Tyr Ala 125											
ttg ttg gaa ctc Leu Leu Glu Leu		Lys Val 1			Trp						
acg tga gtgccgg Thr	cca ccctggca	ga acctgto	caca gtttga	aggca caggctc	gga 658						
aacgaatacc tcca	cgggcc catto	ccgag att	ctagtga tte	ctgctgat ggac	tgggcc 718						
acaccctctg agaa	.ccttgt accct	catct gct	cgtgtgg ata	aageeeee cagt	gtgctg 778						
ccctacttca atac	gteeta eetta	eggee etta	acacctg at	gagtacta gcca	ccacaa 838						
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<210> 69

<211> 1244 <212> DNA <213> Homo sapiens <220> <221> CDS <222> (31)..(1095) <400> 69 tggaagcacg cacagttgtg accatcaagt atg cag gaa gca atc att ctc 51 Met Gln Glu Ala Ile Ile Leu ctg gct ctc ctg ggt gcc atg tca ggg gga gaa gca cta cac cta atc 99 Leu Ala Leu Leu Gly Ala Met Ser Gly Gly Glu Ala Leu His Leu Ile 15 ctc tta cct gct aca ggc aat gtg gca gag aat tct cca cct ggg act 147 Leu Leu Pro Ala Thr Gly Asn Val Ala Glu Asn Ser Pro Pro Gly Thr 25 tca gtg cac aag ttt tct gtg aag tta tca gca tca ttg tca cct gtg 195 Ser Val His Lys Phe Ser Val Lys Leu Ser Ala Ser Leu Ser Pro Val 40 45 atc cca gga ttt ccc cag ata gtc aac tca aat ccc ctc act gaa gct 243 Ile Pro Gly Phe Pro Gln Ile Val Asn Ser Asn Pro Leu Thr Glu Ala ttt agg gtg aat tgg ctg tca ggc acc tac ttt gag gtt gtc acc act 291 Phe Arg Val Asn Trp Leu Ser Gly Thr Tyr Phe Glu Val Val Thr Thr 80 ggg atg gaa caa cta gat ttt gaa aca gga cca aac ata ttt qat ttq Gly Met Glu Gln Leu Asp Phe Glu Thr Gly Pro Asn Ile Phe Asp Leu . 90 95 cag att tat gtg aag gat gag gtt ggt gtc aca gac ctt caa gtc ctg 387 Gln Ile Tyr Val Lys Asp Glu Val Gly Val Thr Asp Leu Gln Val Leu 110 act gtc cag gta aca gat gtg aac gag cca cct cag ttt caa ggc aac 435 Thr Val Gln Val Thr Asp Val Asn Glu Pro Pro Gln Phe Gln Gly Asn 125 ttg gca gaa ggt cta cac ctc tac ata gta gaa aga gca aac cct gga 483 Leu Ala Glu Gly Leu His Leu Tyr Ile Val Glu Arg Ala Asn Pro Gly 140 ttc att tac cag gtt gag gcc ttc gat cca gaa gac aca agc cga aac 531 Phe Ile Tyr Gln Val Glu Ala Phe Asp Pro Glu Asp Thr Ser Arg Asn att ccc ctc agt tat ttc ctg att tct ccc cca aag agc ttc aga atg 579 Ile Pro Leu Ser Tyr Phe Leu Ile Ser Pro Pro Lys Ser Phe Arg Met 175 tot got aat ggc acc ctc ttc tcc aca aca gaa ttg gac ttt gaa gca 627 Ser Ala Asn Gly Thr Leu Phe Ser Thr Thr Glu Leu Asp Phe Glu Ala 190

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gat gat gaa ggt ttt ccc agc cac ctc ctc tac agc att acc act gtt Asp Asp Glu Gly Phe Pro Ser His Leu Leu Tyr Ser Ile Thr Thr Val 265 270 275	867								
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caa agg ata gac cga gat gca ggt gaa ttg aga caa aat ccc acc att Gln Arg Ile Asp Arg Asp Ala Gly Glu Leu Arg Gln Asn Pro Thr Ile 300 305 310	963								
tcc ctg gaa gtt cta gtg aag gac aga cca tat ggg ggt cag gag aat Ser Leu Glu Val Leu Val Lys Asp Arg Pro Tyr Gly Gly Gln Glu Asn 315 320 325	1011								
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		att Ile				_		-		_		_			-	2	2417
		ttc Phe														2	2465
		act Thr	_			_	_		_					_		2	2513
	_	aag Lys 810		_					_	_			_		_	2	2561
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1485

1490

1495

1460

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ggt Gly 30	cct Pro	ggc	tgc Cys	acc Thr	gca Ala 35	tcc Ser	cct Pro	cct Pro	gca Ala	ccc Pro 40	cct Pro	gga Gly	tgg Trp	ccc Pro	ttc Phe 45		204
agc Ser	caa Gln	cgg Arg	ejà aaa	cct Pro 50	Gly aaa	cga Arg	tgg Trp	tcg Ser	acc Thr 55	acg Thr	gag Glu	ctg Leu	cgc Arg	aag Lys 60	gaa Glu		252
aag Lys	tcc Ser	cgg Arg	gat Asp 65	gcg Ala	gcc Ala	cgc Arg	agc Ser	cgg Arg 70	cgc Arg	agc Ser	cag Gln	gag Glu	acc Thr 75	gag Glu	gtg Val		300
ctg Leu	tac Tyr	cag Gln 80	ctg Leu	gct Ala	cac His	acg Thr	ctg Leu 85	ccc Pro	ttc Phe	gcc Ala	cgc Arg	ggc 90	gtc Val	agc Ser	gcc Ala		348
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atg Met 110	cac His	cgc Arg	ctc Leu	tgc Cys	gcc Ala 115	gca Ala	gjå aaa	gag Glu	tgg Trp	aac Asn 120	cag Gln	gtg V al	gga Gly	gca Ala	999 Gly 125		444
gga Gly	gaa Glu	cca Pro	ctg Leu	gat Asp 130	gcc Ala	tgc Cys	tac Tyr	ctg Leu	aag Lys 135	gcc Ala	ctg Leu	gag Glu	ggc ggc	ttc Phe 140	gtc Val		492
atg Met	gtg Val	ctc Leu	acc Thr 145	gcc Ala	gag Glu	gga Gly	gac Asp	atg Met 150	gct Ala	tac Tyr	ctg Leu	tcg Ser	gag Glu 155	aat Asn	gtc Val		540
														agc Ser			588
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														acg Thr			684
cgg Arg	tgc Cya	ttc Phe	tcc Ser	ttg Leu 210	cgc Arg	atg Met	aag Lys	agt Ser	acg Thr 215	ctc Leu	acc Thr	agc Ser	cgc Arg	999 Gly 220	cgc Arg		732
														tct Ser			780
cat His	atg Met	agg Arg 240	gcc Ala	tac Tyr	aag Lys	cca Pro	cct Pro 245	gcg Ala	cag Gln	act Thr	tct Ser	cca Pro 250	gct Ala	gjå aaa	agc Ser		828
														gaa Glu			876

atc ccc cac cca ggc agc ctg gag ccc cca ctg ggc cga ggg gcc ttc Ile Pro His Pro Gly Ser Leu Glu Pro Pro Leu Gly Arg Gly Ala Phe 270 285	924
ctc agc cgc cac agc ctg gac atg aag ttc acc tac tgt gac gac agg Leu Ser Arg His Ser Leu Asp Met Lys Phe Thr Tyr Cys Asp Asp Arg 290 295 300	972
att gca gaa gtg gct ggc tat agt ccc gat gac ctg atc ggc tgt tcc Ile Ala Glu Val Ala Gly Tyr Ser Pro Asp Asp Leu Ile Gly Cys Ser . 305 310 315	1020
gcc tac gag tac atc cac gcg ctg gac tcc gac gcg gtc agc aag agc Ala Tyr Glu Tyr Ile His Ala Leu Asp Ser Asp Ala Val Ser Lys Ser 320 325 330	1068
atc cac acc tgt atg tat ccc att tcc cca ggt gcg aag cca gct gcc Ile His Thr Cys Met Tyr Pro Ile Ser Pro Gly Ala Lys Pro Ala Ala 335 340 345	1116
aca tgg ccc cca gct gac acc agg acc ccc cag ctc ccc ata ccc cag Thr Trp Pro Pro Ala Asp Thr Arg Thr Pro Gln Leu Pro Ile Pro Gln 350 365	1164
gat gca ctg cct ccc cac ctc aac acc agc tcc ctg ctc ccc aag ccc Asp Ala Leu Pro Pro His Leu Asn Thr Ser Ser Leu Leu Pro Lys Pro 370 375 380	1212
caa gga act gtc tcc ttc ctt gcc ccc tca tac cca gtc ccc aga tct Gln Gly Thr Val Ser Phe Leu Ala Pro Ser Tyr Pro Val Pro Arg Ser 385 390 395	1260
ttc tct ccc cat ttg ccc cct tgg tgg ccc tga tccctccc gatccccctc Phe Ser Pro His Leu Pro Pro Trp Trp Pro 400 405	1311
ctcagtgctg agcaagggcc aggcagtaac agggcagtat cgcttcctgg cccggagtgg	1371
tggctacctg tggacccaga cccaggccac agtggtgtca gggggacggg gcccccagtc	1431
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tgt	1494

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<220>

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<222> (131)..(1387)

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ctg Leu 30	tat Tyr	gat Asp	gat Asp	gtg Val	ctg Leu 35	aca Thr	gcc Ala	acc	tca Ser	cag Gln 40	ccc Pro	tca Ser	gat Asp	Asp Bac	aga Arg 45	265
agc Ser	agc Ser	agc Ser	act Thr	gaa Glu 50	cca Pro	cct Pro	cct Pro	cct Pro	gtt Val 55	cgc Arg	cag Gln	gag Glu	cca Pro	tct Ser 60	ccc Pro	313
aag Lys	ccc Pro	aac Asn	aac Asn 65	aag Lys	acc Thr	cct Pro	gca Ala	att Ile 70	ctg Leu	tat Tyr	acc Thr	tac Tyr	agt Ser 75	ggc Gly	ctg Leu	361
cgt Arg	aat Asn	aga Arg 80	cga Arg	gct Ala	gcc Ala	gtt Val	tat Tyr 85	gtg Val	ggc	agc Ser	ttc Phe	tcc Ser 90	tgg Trp	tgg Trp	acc Thr	409
aca Thr	gac Asp 95	cag Gln	cag Gln	ctg Leu	atc Ile	cag Gln 100	gtt Val	att Ile	cgc Arg	tct Ser	ata Ile 105	gga Gly	gtc Val	tat Tyr	gat Asp	457
gtg Val 110	gtg Val	gag Glu	ttg Leu	aaa Lys	ttt Phe 115	gca Ala	gag Glu	aat Asn	cga Arg	gca Ala 120	aat Asn	ggc Gly	cag Gln	tcc Ser	aaa Lys 125	505
61 A 83 B	tat Tyr	gct Ala	gag Glu	gtg Val 130	gtg Val	gta Val	gcc Ala	tct Ser	gaa Glu 135	aac Asn	tct Ser	gtc Val	cac His	aaa Lys 140	ttg Leu	553
Leu	gaa Glu	Leu	Leu 145	Pro	Gly	Lys	Val	Leu 150	Asn	Gly	Glu	Lys	Val 155	Asp	Val	601
Arg	ccg Pro	Ala 160	Thr	Arg	Gln	Asn	Leu 165	Ser	Gln	Phe	Glu	Ala 170	Gln	Ala	Arg	649
aaa Lys	cgt Arg 175	gag Glu	tgt Cys	gtc Val	cga Arg	gtc Val 180	cca Pro	aga Arg	ejà aaa	gga Gly	ata Ile 185	cct Pro	cca Pro	cgg Arg	gcc Ala	697
cat His 190	tcc Ser	cga Arg	gat Asp	tct Ser	agt Ser 195	gat Asp	tct Ser	gct Ala	gat Asp	gga Gly 200	cgg Arg	gcc Ala	aca Thr	ccc Pro	tct Ser 205	745
Glu	aac Asn	Leu	Val	Pro 210	Ser	Ser	Ala	Arg	Val 215	Asp	Lys	Pro	Pro	Ser 220	Val	793
Leu	ccc Pro	Tyr	Phe 225	Asn	Arg	Pro	Pro	Ser 230	Ala	Leu	Pro	Leu	Met 235	Gly	Leu	841
acc	cca	cca	cca	att	cca	ccc	cca	cca	cct	ctc	tcc	tca	agc	ttt	9 99	889

Pro	Pro	Pro 240	Pro	Ile	Pro	Pro	Pro 245	Pro	Pro	Leu	Ser	Ser 250	Ser	Phe	Gly		
_						~~							atg Met			9	937 [°]
		_						-	_				gjà aaa	_		<u> </u>	985
		-						_			_	_	cca Pro		_	10	033
									-	_	_		gçc Ala 315			10	081
				_	_	_	_						aca Thr		_	1:	129
_	_	-		_	_		_	_	_		_	_	att Ile		_	1:	177
_	_				_	_			_	_	_		gat Asp		_	13	225
													aaa Lys			1:	273
					_								tct Ser 395			1:	321
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	_		tcc Ser		tga	g										1:	388

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<213> Homo sapiens

<220>

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<222> (40)..(2124)

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tcg Ser	gag Glu	tcc Ser	ttg Leu 25	gjå aaa	acg Thr	gag Glu	cag Gln	cgc Arg 30	gtc Val	gtg Val	gj aaa	cga Arg	gcg Ala 35	gca Ala	gaa Glu	150
		ggc Gly 40														198
gly ggg	gat Asp 55	gct Ala	gtg Val	gag Glu	ctg Leu	agc Ser 60	tgt Cys	ccc Pro	ccg Pro	ccc Pro	e2 e1Å aaa	ggt Gly	ggt Gly	ccc Pro	atg Met	246
999 Gly 70	ccc Pro	act Thr	gtc Val	tgg Trp	gtc Val 75	aag Lys	gat Asp	ggc Gly	aca Thr	80 GJA aaa	ctg Leu	gtg Val	ccc Pro	tcg Ser	gag Glu 85	294
		ctg Leu														342
		tcc Ser														390
		cac His 120														438
		gac Asp														486
gcc Ala 150	cct Pro	tac Tyr	tgg Trp	aca Thr	cgg Arg 155	ccc Pro	gag Glu	cgg Arg	atg Met	gac Asp 160	aag Lys	aag Lys	ctg Leu	ctg Leu	gcc Ala 165	534
gtg Val	ccg Pro	gcc Ala	gcc Ala	aac Asn 170	acc Thr	gtc Val	cgc Arg	ttc Phe	cgc Arg 175	tgc Cys	cca Pro	gcc Ala	gct Ala	ggc Gly 180	aac Asn	582
		ccc Pro														630
		cgc Arg 200														678
gtc Val	atg Met 215	gaa Glu	agc Ser	gtg Val	gtg Val	ccc Pro 220	tcg Ser	gac Asp	cgc Arg	ggc Gly	aac Asn 225	tac Tyr	acc Thr	tgc Cys	gtc Val	726
gtg	gag	aac	aag	ttt	ggc	agc	atc		cag	acg	tac	acg	ctg	gac	gtg	774

Val 230	Glu	Asn	ъ̀уѕ	Phe	Gly 235	Ser	Ile	Arg	Gln	Thr 240	Tyr	Thr	Leu	Asp	Val 245	
	gag Glu															822
	cag Gln															870
	agt Ser	_	_	_				_			_					918
	ggc Gly 295	_	_			_	_					_				966
_	gtg Val		_				_		_	_					_	1014
	cgc Arg				-							_	_	_		1062
_	tcc Ser				_		_	_								1110
	cgg Arg															1158
	gtc Val 375															1206
	gtc Val															1254
	ctg Leu															1302
aaa Lys	cac His	aaa Lys	aac Asn 425	atc Ile	atc Ile	aac Asn	ctg Leu	ctg Leu 430	Gly ggc	gcc Ala	tgc Cys	acg Thr	cag Gln 435	gly ggc	gjå aaa	1350
	ctg Leu			_					_	-			_			1398
	ctg Leu 455															1446
	aag Lys															1494

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atc cac agg Ile His Arg	gac ctg gct gcc Asp Leu Ala Ala 505	cgc aat gtg ctg gtg acc Arg Asn Val Leu Val Thr 510	gag gac aac 1590 Glu Asp Asn 515
	Ile Ala Asp Phe	ggg ctg gcc cgg gac gtg Gly Leu Ala Arg Asp Val 525 530	. His Asn Leu
		aac ggc cgg ctg ccc gtg Asn Gly Arg Leu Pro Val 545	
		cga gtc tac act cac cag Arg Val Tyr Thr His Gln 560	
tgg tcc ttt Trp Ser Phe	ggg gtc ctg ctc Gly Val Leu Leu 570	tgg gag atc ttc acg ctg Trp Glu Ile Phe Thr Leu 575	g ggg ggc tcc 1782 Gly Gly Ser 580
		gag gag ctc ttc aag ctg Glu Glu Leu Phe Lys Leu 590	
	Met Asp Lys Pro	gcc aac tgc aca cac gac Ala Asn Cys Thr His Asp 605 610	Leu Tyr Met
		gcc gcg ccc tcc cag agg Ala Ala Pro Ser Gln Arg 625	
		gac cgt gtc ctt acc gtg Asp Arg Val Leu Thr Val 640	
		gcg cct ttc gag cag tac Ala Pro Phe Glu Gln Tyr 655	
		age tee tea ggg gae gae Ser Ser Ser Gly Asp Asp 670	
	Leu Leu Pro Pro	gcc cca ccc agc agt ggg Ala Pro Pro Ser Ser Gly 685 690	Gly Ser Arg
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tgctggtgca			2184

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                                                                     120
ccttcttccc ctcacatgtg gggactttta attccatgta tattaggctg catgaagctt
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ccccacaacc tactgatgct cttttcatta gaaacatttc ttactctgcg tttcattttg
                                                                     240
gatagtttct attcctatgt tttcaaaccc accaataaaa gattctgcaa catctgacct
                                                                     300
gccattaatc ccgtccagtg tatttttcat ctcctgtatt gtagttttca tctctacaat
                                                                     360
ccagcttgag cctttggtta tatcttccat gttgctcctg cactgtttga acatgcagaa
                                                                     420
tggctagtgg ggcagtgagc tgaggagaag ggacagaggg gaagctcggc tgttgggtct
                                                                     480
         atg atg gag acc atg cag ctg aaa gta aac cgt cac ccc ttc
                                                                     528
acgggt
         Met Met Glu Thr Met Gln Leu Lys Val Asn Arg His Pro Phe
tgc ttc agt gtg aaa ggc cag gtg aag atg ctg cag ctg atg agg ctg
                                                                     576
Cys Phe Ser Val Lys Gly Gln Val Lys Met Leu Gln Leu Met Arg Leu
ggc ctt agg gtg cgg ggg gtg gta tct gct tgt.ggg cgg gag atg
                                                                     624
Gly Leu Arg Val Arg Gly Val Val Glu Ser Ala Cys Gly Arg Glu Met
tgg cta tgt ggc tat aaa gga tga agatgaacgc cctgtttgct tttcagcctc
                                                                     678
Trp Leu Cys Gly Tyr Lys Gly
             50
gcttggatca aggttaaaag gccggttgtg gccttcttgg tggaagaaag agagagataa
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<213> Homo sapiens
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ctc ctt tta ctg gca ttc cag ctc cta ggt cag acc aga gct aat ccc Leu Leu Leu Ala Phe Gln Leu Leu Gly Gln Thr Arg Ala Asn Pro 15 20 25	160
atg tac aat gcc gtg tcc aac gca gac ctg tta ctg aaa gtg gtt tga Met Tyr Asn Ala Val Ser Asn Ala Asp Leu Leu Leu Lys Val Val 30 35 40	208
aagtgaataa acttcagcac catggacaga agacaaatgc ctgcgttggt gtgctttctt	268
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agaatgctga gtttttcttc ttcctttca	357
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att tgt gcc agt gga caa ccc cgg ggt aat cag ttg aaa gga gag aac Ile Cys Ala Ser Gly Gln Pro Arg Gly Asn Gln Leu Lys Gly Glu Asn 15 20 25	160
tac tcc ccc agg tat atc tgc agc att cct ggc ttg cct gga cct cca Tyr Ser Pro Arg Tyr Ile Cys Ser Ile Pro Gly Leu Pro Gly Pro Pro 30 35 40	208
ggg ccc cct gga gca aat ggt tcc cct ggg ccc cat ggt cgc atc ggc Gly Pro Pro Gly Ala Asn Gly Ser Pro Gly Pro His Gly Arg Ile Gly 45 50 55	256
ctt cca gga aga gat ggt aga gac ggc agg aaa gga gag aaa ggt gaa Leu Pro Gly Arg Asp Gly Arg Asp Gly Arg Lys Gly Glu Lys Gly Glu 60 65 70 75	304
aag gga act gca ggt ttg aga ggt aag act gga ccg cta ggt ctt gcc Lys Gly Thr Ala Gly Leu Arg Gly Lys Thr Gly Pro Leu Gly Leu Ala	352

ggt gag aaa ggg gac caa gga gag act ggg aag aaa gga ccc ata gga Gly Glu Lys Gly Asp Gln Gly Glu Thr Gly Lys Lys Gly Pro Ile Gly 95 100 105	400
cca gag gga gag aaa gga gaa gta ggt cca att ggt cct cct gga cca Pro Glu Gly Glu Lys Gly Glu Val Gly Pro Ile Gly Pro Pro Gly Pro 110 115 120	448
aag gga gac aga gga gaa caa ggg gac ccg ggg ctg cct gga gtt tgc. Lys Gly Asp Arg Gly Glu Gln Gly Asp Pro Gly Leu Pro Gly Val Cys 125 130 135	496
aga tgt gga agc atc gtg ctc aaa tcc gcc ttt tct gtt ggc atc aca Arg Cys Gly Ser Ile Val Leu Lys Ser Ala Phe Ser Val Gly Ile Thr 140 145 150 155	544
acc agc tac cca gaa gaa aga cta cct att ata ttt aac aag gtc ctc Thr Ser Tyr Pro Glu Glu Arg Leu Pro Ile Ile Phe Asn Lys Val Leu 160 165 170	592
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aag cat ctg gca atc gga ctg gta cac aat ggg caa tac cgg ata aag Lys His Leu Ala Ile Gly Leu Val His Asn Gly Gln Tyr Arg Ile Lys 205 210 215	736
acc ttc gac gcc aac aca gga aac cat gat gtg gct tcg ggg tcc aca Thr Phe Asp Ala Asn Thr Gly Asn His Asp Val Ala Ser Gly Ser Thr 220 235 230 235	784
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aca gac cag aat ggc ctc ttc tca gac cca ggt tgg gca gac agc tta Thr Asp Gln Asn Gly Leu Phe Ser Asp Pro Gly Trp Ala Asp Ser Leu 255 260 265	880
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aaataaaaaa aaaaaa 1297

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		21> 0	DS (189)	(7	(01)											
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ttco	cgcc	etc t	ccga	cccc	g to	ctcac	etteg	cto	cctgg	gca	gctg	cgcg	gga g	gaact	ggggc	180
tcad	cgto		Asp				Glu					Phe			aac Asn	230
	_		_			-								ttt Phe		278
														gca Ala 45		326
														aaa Lys		374
		_	_		_			_			_			ctt Leu	_	422
														aac Asn		470
			-	_			_							gat Asp		518
														gtg Val 125		566
														gat Asp		614
														tta Leu		662

agt ttt ata Ser Phe Ile 160			_		aggagtcc	711
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aaataatctc t	tgcaggttt	ttcacttgtt	aatattaggt	agtacttctt	atcacaaata	891
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<210> 79

<211> 1370

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<213> Homo sapiens

<220>

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<222> (302)..(940)

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634

get gtc atc gca gcc atc atc tcc agg gaa agc cat ggc gga tct gtc

Ala Val Ile Ala Ala Ile Ile Ser Arg Glu Ser His Gly Gly Ser Val 100 105 110	
ctg caa gac ggc tgg gac cac agg gga ctt aaa ttt ggc ttg atg cag Leu Gln Asp Gly Trp Asp His Arg Gly Leu Lys Phe Gly Leu Met Gln 115 120 125	682
ctt gat aaa caa acg tac cac cct gtc ggt gcc tgg gat agc aaa gag Leu Asp Lys Gln Thr Tyr His Pro Val Gly Ala Trp Asp Ser Lys Glu 130 135 140	730
Cac ctt tca cag gct act ggg att cta aca gag aga att aag gca atc His Leu Ser Gln Ala Thr Gly Ile Leu Thr Glu Arg Ile Lys Ala Ile 145 150 155	778
Cag aaa aaa ttc ccc acg tgg agt gtt gct cag cac ctc aaa ggt ggt Gln Lys Lys Phe Pro Thr Trp Ser Val Ala Gln His Leu Lys Gly Gly 160 165 170 175	826
ctc tca gct ttt aag tca gga att gaa gcg att gcc acc cca tcg gac Leu Ser Ala Phe Lys Ser Gly Ile Glu Ala Ile Ala Thr Pro Ser Asp 180 185 190	874
ata gac aat gac ttc gtc aat gat atc att gct cga gct aag ttc tat Ile Asp Asn Asp Phe Val Asn Asp Ile Ile Ala Arg Ala Lys Phe Tyr 195 200 205	922
aaa aga caa agc ttc tag gcaaag ctctgtgggt gggccaggtt ggcagagtgc Lys Arg Gln Ser Phe 210	976
tcagatggcc gcctttgaga gttttacgtg aatgtgttgt atacaacact ggcacagaaa	1036
tgattaaaat catgaaagaa aattcatttc ccaattttct gaatgaaaat aatcattgaa	1096
aaaaggaaag aaaaataaaa gaaatccatc cagttcacaa tatggttcct aggaaacgga	1156
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cagaattgct aacaagttaa gtaagcctta cccgagcctt tgtctttttt ccagtatctg	1336
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<221> CDS <222> (161)..(1906)

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ccccgageca ggeetteege eacegeeeee gggeeatgge ecccegeege eaceetteet 120

egegeggeee ggeeeg	geggg geteceggee go	Met	g gtg ttc cgc aac 175 t Val Phe Arg Asn 1 5
	ccg gag gag gag gac Pro Glu Glu Glu Asg 10		
	ctg ctg tgt ccc cgg Leu Leu Cys Pro Arg 30	His Arg Cys	
	ccg ggc ttg gcg cto Pro Gly Leu Ala Leu 45		
	gcg cag ttg gcg gct Ala <u>G</u> ln Leu Ala Ala 60		
	aag aca gtc ggt ggg Lys Thr Val Gly Gly 75		
	cec cet ceg cag cec Pro Pro Pro Gln Pro 90		
	gac ccc acg gaa acg Asp Pro Thr Glu Thi 110	Ser Asp Ala	
	tcg gag gcc gag ago Ser Glu Ala Glu Sec 125		
	agc agc ccg ggt cgc Ser Ser Pro Gly Arg 140		
	ccc cca ggc cct gas Pro Pro Gly Pro Glo 155	_	
Leu Gln Asp Leu	gtc cct ctg ggg cgc Val Pro Leu Gly Ar 170		
2	cag caa cct ccc cc Gln Gln Pro Pro Pro 19	o Pro Pro Pro	
	gcg ggt cct tct cg Ala Gly Pro Ser Ar 205		
	ttt cgc acc aag ag Phe Arg Thr Lys Se 220		Gly Ser Gly Gly

١

999 Gly 230	Asp	Gly gg5	acc Thr	ggc	aag Lys 235	agg Arg	cct Pro	tct Ser	gga Gly	gag Glu 240	Leu	g gct L Ala	gct Ala	tca Ser	gct Ala 245	895
gcg Ala	ago Ser	ctg Leu	aca Thr	gac Asp 250	Met	gga Gly	Gly	tct Ser	gcg Ala 255	Gly	cgc	g gag g Glu	ctg Leu	gac Asp 260	gcg	943
GJ A BBB	agg Arg	aaa Lys	ccc Pro 265	Lys	ttg Leu	aca Thr	aga Arg	act Thr 270	Gln	agt Ser	gcc	ttt Phe	tct Ser 275	Pro	gtc Val	991
tcc Ser	ttc Phe	ago Ser 280	ccc Pro	ctg Leu	ttc Phe	aca Thr	ggt Gly 285	Glu	act Thr	gtg Val	tcg Ser	ctt Leu 290	Val	gat Asp	gtg Val	1039
gac Asp	att Ile 295	tct Ser	cag Gln	cgg Arg	ggc	ctg Leu 300	acc Thr	tct Ser	cca Pro	cac His	cct Pro 305	Pro	act Thr	ccc Pro	cct Pro	1087
cct Pro 310	cct Pro	ccg Pro	aga Arg	aga Arg	agc Ser 315	ctc Leu	agc Ser	ctc Leu	cta Leu	gat Asp 320	gat Asp	atc Ile	agt Ser	ejy aaa	acg Thr 325	1135
ctg Leu	cct Pro	aca Thr	tct Ser	gtc Val 330	ctt Leu	gtg Val	gct Ala	ecg Pro	atg Met 335	eja aaa	tct Ser	tcc Ser	Leu	cag Gln 340	tct Ser	1183
ttc Phe	ccc Pro	cta Leu	cct Pro 345	ccg Pro	cct Pro	cct Pro	cca Pro	ccc Pro 350	cat His	gcc Ala	cca Pro	gat Asp	gca Ala 355	ttt Phe	ccc Pro	1231
cgg Arg	att Ile	gct Ala 360	ccc Pro	atc Ile	cga Arg	gca Ala	gct Ala 365	gaa Glu	tcc Ser	ctg Leu	cac His	agc Ser 370	caa Gln	ccc Pro	cca Pro	1279
cag Gln	cac His 375	ctc Leu	cag Gln	tgt Cys	ccc Pro	ctc Leu 380	tac Tyr	cgg Arg	cct Pro	gac Asp	tcg Ser 385	agc Ser	agc Ser	ttt Phe	gca Ala	1327
gcc Ala 390	agc Ser	ctt Leu	cga Arg	gag Glu	ttg Leu 395	gag Glu	aag Lys	tgt Cys	ggt Gly	tgg Trp 400	tat Tyr	tgg Trp	gjå aaa	cca Pro	atg Met 405	1375
aat Asn	tgg Trp	gaa Glu	gat Asp	gca Ala 410	gag Glu	atg Met	aag Lys	ctg Leu	aaa Lys 415	G1A aaa	aaa Lys	cca Pro	gat Asp	ggt Gly 420	tct Ser	1423
ttc Phe	ctg Leu	gta Val	cga Arg 425	gac Asp	agt Ser	tct Ser	gat Asp	cct Pro 430	cgt Arg	tac Tyr	atc Ile	ctg Leu	agc Ser 435	ctc Leu	agt Ser	1471
ttc Phe	cga Arg	tca Ser 440	cag Gln	ggt Gly	atc Ile	Thr	cac His 445	cac His	act Thr	aga Arg	atg Met	gag Glu 450	cac His	tac Tyr	aga Arg	1519
gga Gly	acc Thr 455	ttc Phe	agc Ser	ctg Leu	\mathtt{Trp}	tgt Cys 460	cat His	ccc Pro	aag Lys	ttt Phe	gag Glu 465	gac Asp	cgc Arg	tgt Cys	caa Gln	1567
tct	gtt	gta	gag	ttt	att	aag	aga	gcc	att	atg	cac	tcc	aag	aat	gga	1615

Ser 470	Val	Val	Glu	Phe	Ile 475	Lys	Arg	Ala	Ile	Met 480	His	Ser	Lys	Asn	Gly 485	
		ctc Leu														1663
		cag Gln	_				_		_		_		_			1711
	_	cac His 520		_	_				_	_		_			_	1759
		cca Pro														1807
_		tac Tyr			_		_	_		_		-			_	1855
		cag Gln														1903
tag	cgaç	999	gctco	cctg	ctgg	gtcad	ca d	ccaag	ggca	at t	ggtt	gcca	a ago	ctcca	agct	1960

<210> 81 <211> 1774

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (313)..(576)

<400> 81

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caagaatctt ttttggcctc tgcctaacca gattcctcct gcctccaggt agattttata 240
cttatttcaa ggcagaaact tggtggaagg aggtaatctg tcgctaatgt gtatttattc 300

60

gggtcgaccc acgogtccgg ctttctattg tatgccacag ttttgcactt ttttgcttta

cttcatgcat gt atg cat tca tac cct ggg att ttt ttc ttc cct tta 348

Met His Ser Tyr Pro Gly Ile Phe Phe Pro Leu 1 5 10

gct gtg ttc cag atc atc tcc ctg gta att tac ccc gtg aag tac acc

Ala Val Phe Gln Ile Ile Ser Leu Val Ile Tyr Pro Val Lys Tyr Thr

15 20 25

cag acc ttc acc ctt cac gat aac cct gct gtt aat tac atc tat aac Gln Thr Phe Thr Leu His Asp Asn Pro Ala Val Asn Tyr Ile Tyr Asn 30 35 40	444
tgg gcc tat ggc ttc gga tgg gcg gcc acc atc atc ttg att ggt tgt Trp Ala Tyr Gly Phe Gly Trp Ala Ala Thr Ile Ile Leu Ile Gly Cys 50 55 60	492
Ser Phe Phe Cys Cys Leu Pro Asn Tyr Glu Asp Asp Leu Leu Gly 65 70 75	540
gcc gcc aag ccc agg tac ttc tat ccc cca gcc taa tgtg ggaggaagag Ala Ala Lys Pro Arg Tyr Phe Tyr Pro Pro Ala 80 85	590
cctgagaaaa gcctgctgca agatggatct gaggaggaaa ctgttctcca aggcacaagg	650
aacctacgtt tgggcaatgt tcatatgatc agaaatgcta gaataaatgc taaagaaaat	710
tcttcataat tagtgttaag tttcatgtat gtcgtgtgga gttaaaaaga cttgaattct	770
gtttgctaag tatatgctaa tttttcctta tgtcaattct ataccattta agcttcattt	830
gttaaagaat atgcctgtga aacttgataa ggtagaaatg tagcagcctc tcatttaata	890
atctgatggg gcttctgttt ttccacatag aatgggttgt ttctgctaag ggctacagag	950
gaggaaagtc actggcaaaa cttccgtgac caaatatcct gaaattagta ttttttaaa	1010
aagaccttat tttgagtttt cagttacata aaaaagcaga agcagattgg tttcctaagt	1070
gagcatcgtt tgtgagaatt tttagtcagt gttttgaaca attattgttt ttctaagctt	1130
cgtgttgact ttctctgatg cgtagaaaag tgttctaacg tagccaaggt taagccgctg	1190
tcactactga aatgctaaga attttcctct tttcccgtag tgtagagggg tagggtgtgg	1250
gaagaageeg tgttageaca tetgtagtat tetgtgtgta tgettagaac cagegtagae	1310
cggatgggag gatggactag gcctaatccc tcccaactgg tggatgtgaa gaggtcaggt	1370
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acatggcagt gtttcttctc agtgcttctt cccttaactg agctctgctc acagacagct	1490
agaatagatt ttaactgtaa cagaaaccta aatgtaatta aaacctggtc ttccttggta	1550
agcagactta aaatatctgt atagtacatg caagtggaaa atttgggaat gcgtgtctct	1610
gaatacatac cggaagggct actattacct tttccttacc atttatactt acctaatgga	1670
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ttttgattag gaagtgggg aataaagag gtgttgaaaa aaaa	1774

<210> 82

<211> 1870 <212> DNA <213> Homo sapiens <220> <221> CDS <222> (91)..(672) <400> 82 tttagtegeg gtgtcagege tegeaggace actettggee getgeteetg eeeggegtte 60 ctccgctccg cgcccgccgc caccgacgac atg ctg cgc tgc ggc ctg gcc 111 Met Leu Arg Cys Gly Leu Ala tgc gag egc tgc agg tgg atc etg ecc etg etc etc age gec atc 159 Cys Glu Arg Cys Arg Trp Ile Leu Pro Leu Leu Leu Ser Ala Ile 207 gcc ttc gac atc atc gcg ctg gcc ggc cgc ggc tgg ctg cag tct agc Ala Phe Asp Ile Ile Ala Leu Ala Gly Arg Gly Trp Leu Gln Ser Ser 30 255 aac cac atc cag aca tcg tcg ctt tgg tgg agg tgt ttc gac gag ggc Asn His Ile Gln Thr Ser Ser Leu Trp Trp Arg Cys Phe Asp Glu Gly 303 ggc ggc agc ggc tcc tac gac gat ggc tgc cag agc ctc atg gag tac Gly Gly Ser Gly Ser Tyr Asp Asp Gly Cys Gln Ser Leu Met Glu Tyr 60 65 gca tgg gga cga gct gca gcc acg ctt ttc tgt ggc ttt atc atc 351 Ala Trp Gly Arg Ala Ala Ala Thr Leu Phe Cys Gly Phe Ile Ile 399 ctg tgc atc tgc ttc att ctc tcg ttc ttc gcc ctg tgt gga ccc cag Leu Cys Ile Cys Phe Ile Leu Ser Phe Phe Ala Leu Cys Gly Pro Gln 447 atg ctt gtt ttc ctg aga gtc att gga ggc ctc ctc gca ctg gct gcc Met Leu Val Phe Leu Arg Val Ile Gly Gly Leu Leu Ala Leu Ala Ala 105 110 495 ata ttc cag atc atc tcc ctg gta att tac ccc gtg aag tac acc cag Ile Phe Gln Ile Ile Ser Leu Val Ile Tyr Pro Val Lys Tyr Thr Gln 120 acc ttc acc ctt cac gat aac cct gct gtt aat tac atc tat aac tgg 543 Thr Phe Thr Leu His Asp Asn Pro Ala Val Asn Tyr Ile Tyr Asn Trp 140 gcc tat ggc ttc gga tgg gcc gcc acc atc atc ttg att ggt tgt tcc 591 Ala Tyr Gly Phe Gly Trp Ala Ala Thr Ile Ile Leu Ile Gly Cys Ser 155 160 ttc ttc ttc tgc tgc ctc ccc aac tac gag gat gac ctt ttg ggg gcc 639 Phe Phe Cys Cys Leu Pro Asn Tyr Glu Asp Asp Leu Leu Gly Ala 170 690 gcc aag ccc agg tac ttc tat ccc cca gcc taa tgtgggag gaagagcctg

Ala Lys Pro Arg Tyr Phe Tyr Pro Pro Ala 185 190

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tacgtttggg	caatgttcat	atgatcagaa	atgctagaat	aaatgctaaa	gaaaattctt	810
cataattagt	gttaagtttc	atgtatgtcg	tgtggagtta	aaaagacttg	aattctgttt	870
gctaagtata	tgctaatttt	tccttatgtc	aattctatac	catttaagct	tcatttgtta	930
aagaatatgc	ctgtgaaact	tgataaggta	gaaatgtagc	agcctctcat	ttaataatct	990
gatggggctt	ctgtttttcc	acatagaatg	ggttgtttct	gctaagggct	acagaggagg	1050
aaagtcactg	gcaaaacttc	cgtgaccaaa	tatcctgaaa	ttagtatttt	tttaaaaaga	1110
ccttattttg	agttttcagt	tacataaaaa	agcagaagca	gattggtttc	ctaagtgagc	1170
atcgtttgtg	agaattttta	gtcagtgttt	tgaacaatta	ttgtttttct	aagcttcgtg	1230
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agcttgtttt	aactatcaga	acactatttt	gtaaggtgct	gcaaagacag	ttgaagtttt	1830
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<220>

<221> CDS

<222> (647)..(910)

<400> 83

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taggaaacct taagctaaaa taagtaacca agagagaatt actcatccta ttcagtctca 180

<211> 1294

<212> DNA

<213> Homo sapiens

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atttgcagta ggactatata ctgtagcacc ctcagggtaa aatatcagac acagaatctc	360
aattaccata gcattteget taattattat eeteatageg ggaataatgg ttactaacag	420
aaaataacac atgggcettt ccaaaccage acetetgeet ettattagga aaggaatgtt	480
gtttctatat cagccaatca gacctagtaa aaagcgctat taaaaaaaac aagctaaaaa	540
gctaaggagt accaaaacaa acaaacagat tcttggtttg ggaacaaaat catagatagc	600
atgggtcatc ccattcctgg gccctctcct aataatatac ctaatt atg gga cta Met Gly Leu 1	655
atg ttc tta ccc tgc cta att aac ctt ttt cag aga ttt ttt aaa ctg Met Phe Leu Pro Cys Leu Ile Asn Leu Phe Gln Arg Phe Phe Lys Leu 5 10 15	703
aca gga tca tgg cca ttt cac aga caa cta ccc aaa aat atc tac aga Thr Gly Ser Trp Pro Phe His Arg Gln Leu Pro Lys Asn Ile Tyr Arg 20 25 30 35	751
cgg cac tgc tcc tac caa cac gat acc aga gaa ctc tct gtc ccc tcg Arg His Cys Ser Tyr Gln His Asp Thr Arg Glu Leu Ser Val Pro Ser 40 45 50	799
tca gca gga agt agc cag aaa gaa cat gcc gcc cct cgt cct ttt tat Ser Ala Gly Ser Ser Gln Lys Glu His Ala Ala Pro Arg Pro Phe Tyr 55 60 65	847
aac tat gag gtc tgg att gac aga gca gaa gca tca cca ttg tgg ata Asn Tyr Glu Val Trp Ile Asp Arg Ala Glu Ala Ser Pro Leu Trp Ile 70 75 80	895
agc gcc tca ttt taa aattcacctt aatcaaaaac tgcctaaatc caaagggcat Ser Ala Ser Phe 85	950
cagectaatg getaaggtea geatgateae aaaceaeaaa taacatetee aaceaaaaae	1010
attccagaca cctcccacag agaaatgcta gcctcgggat aacccctctc ctgccggaaa	1070
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ctcccccaca cagaaacatt ccaagettgt aataagetee etcaeeetaa aaccaaegta	1190
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<210> 84

<211> 633 <212> DNA

<213> Homo sapiens	
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ttg tca ata ata tgg aaa aat ttg ata ttt cat cag gaa tat gaa cat Leu Ser Ile Ile Trp Lys Asn Leu Ile Phe His Gln Glu Tyr Glu His 10 15 20	19
gtg ttt cag gta gag aat gcc aaa gat aat gaa gat agt att cta caa Val Phe Gln Val Glu Asn Ala Lys Asp Asn Glu Asp Ser Ile Leu Gln 25 30 35 40	67
aga gaa att cct gcc aga caa tcc cga aga aga ttt cgg aaa att aac Arg Glu Ile Pro Ala Arg Gln Ser Arg Arg Arg Phe Arg Lys Ile Asn 45 50 55	15
tat aaa gga gag cgc caa acc att act gat gat gtg gag gtt aac agc Tyr Lys Gly Glu Arg Gln Thr Ile Thr Asp Asp Val Glu Val Asn Ser 60 65 70	63
tat ctt tct gtg agt ata ttt agg aac act tca tga atct tccttaattt Tyr Leu Ser Val Ser Ile Phe Arg Asn Thr Ser 75 80	13
tcatatctag tatctttaat ttacatgtat ctttggtaat atcaacatgc tgggctctgt 4	73
atgtgaaaat ttggggcagg taaatatata atctttttaa atgcttctgt ttggttgaat 5:	33
tggttaggaa tgctcttacc agtgggaggt ctggttttgc ttttttgttg gtggctaaac 59	93
agegaaaaaa ectattagge tggatgeace gggteatgee 63	33
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<220> <221> CDS <222> (184)(2172)	
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205

gtcagatgtg ccaccccgcc acaactggcc aatggggtga cggaaggcct ggactatggc

60

120

180

ttc	_	Lys	_	_		Phe		_			Gly			_	cac His	228
	gct Ala					_	-		_					_		276
	cct Pro															324
	ggt Gly															372
	cag Gln 65	_					_							_	_	420
	ctc Leu															468
	aga Arg															516
gat Asp	ttt Phe	gac Asp	tgt Cys 115	gga Gly	aag Lys	gca Ala	gcc Ala	cgg Arg 120	att Ile	cag Gln	tgc Cys	ttc Phe	aaa Lys 125	ggc Gly	ttc Phe	564
	ctc Leu															612
agc Ser	tct Ser 145	GJÀ aaa	ttc Phe	cac His	cac His	ttt Phe 150	gaa Glu	cac His	act Thr	tct Ser	tgt Cys 155	ggt Gly	tct Ser	ctt Leu	cca Pro	660
	ata Ile															708
gtg V al	ata Ile	act Thr	tac Tyr	agc Ser 180	tgc Cys	agg Arg	tct Ser	gga Gly	tat Tyr 185	gtc Val	ata Ile	caa Gln	Gly	agt Ser 190	tca Ser	756
gat Asp	ctg Leu	att Ile	tgt Cys 195	aca Thr	gag Glu	aaa Lys	Gly 999	gta Val 200	tgg Trp	agc Ser	cag Gln	cct Pro	tat Tyr 205	cca Pro	gtc Val	804
tgt Cys	gag Glu	ccc Pro 210	Leu	tcc Ser	tgt Cys	Gly aaa	tcc Ser 215	cca Pro	ccg Pro	tct Ser	gtc Val	gcc Ala 220	aat Asn	gca Ala	gtg Val	852
gca Ala	act Thr 225	Gly	gag Glu	gca Ala	cac His	acc Thr 230	Tyr	gaa Glu	agt Ser	gaa Glu	gtg Val 235	aaa Lys	ctc Leu	aga Arg	tgt Cys	900

ctg Leu 240	GLu	ggt Gly	tat Tyr	acg Thr	atg Met 245	Asp	aca	gat Asp	acc Thr	aga Arg 250	Ser	ato : Ile	acc Thr	tgt Cys	cag Gln 255	948
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tgt Cys	cct Pro	cto Leu	ccg Pro 275	gaa Glu	aac Asn	ata Ile	aca Thr	cat His 280	Ile	ctt Leu	gta Val	cat His	999 Gly 285	gac Asp	gat Asp	1044
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)

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445

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	Thr					Asn					Glu			ggc		3267
Pro					Gln					Ser				gag Glu		3315
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ccc act atg ggt gcc cct aag act gtg gac gag aag gcc ttc ttt gac Pro Thr Met Gly Ala Pro Lys Thr Val Asp Glu Lys Ala Phe Phe Asp 1820 1825 1830 1835	5523
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175

821

cgc ctg gag caa ccc ttc ctg gac ctc aag aac atc gtg ttg acc acc

Arg Leu Glu Gln Pro Phe Leu Asp Leu Lys Asn Ile Val Leu Thr Thr

155

170

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_	_	_	_	_	_		_	att Ile	_		_	_				965
	_				_	_	_	aaa Lys				_			-	1013
	_	_		_				aat Asn								1061
_	_			_				act Thr		_			_	_		1109
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		_				_		aac Asn		_					-	1205
		_	_		_	_		cca Pro		_					_	1253
		_			_			atc Ile			_		_	_	_	1301
	_	_		_			_	cgc Arg	_		_					1349
		_			_			ttt Phe 365	_			-				1397
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								tct Ser								1493
								agg Arg								1541
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Ser	Gly	Val	Val	Leu 425	Asp	Thr	Gly	Val	Ser 430	Gly	Arg	Gly	Glu	Ala 435	Pro	
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gct Ala	gat Asp	cag Gln 455	ccc Pro	tgg Trp	gaa Glu	ggc Gly	aca Thr 460	gga Gly	cgt Arg	ggt Gly	gct Ala	gcc Ala 465	cag Gln	gca Ala	aag Lys	1685
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Thr Gly Leu Gly Leu Lys Val Leu Gly Gly Ile Asn Arg Asn Glu Gly
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cca ttg gta tat att cag gaa att att cct gga gga gac tgt tat aag
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25 30 35

gat ggt cgt ttg aag cca gga gat caa ctt gtc tca gtc aac aag gaa 256
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40 45 50 55

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Ser Met Ile Gly Val Ser Phe Glu Glu Ala Lys Ser Ile Ile Thr Arg
60 65 70

gcc aag ttg agg tta gaa tct gct tgg gag ata gca ttc ata aga caa 352 Ala Lys Leu Arg Leu Glu Ser Ala Trp Glu Ile Ala Phe Ile Arg Gln 75 80 85

aaa tcc gac aac att cag cca gaa aat ctg tca tgt aca tca ctt ata 400 Lys Ser Asp Asn Ile Gln Pro Glu Asn Leu Ser Cys Thr Ser Leu Ile

		90					95					100				
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tct Ser 120	tct Ser	cct Pro	cct Pro	gaa Glu	ata Ile 125	cta Leu	atc Ile	cca Pro	aag Lys	acc Thr 130	tca Ser	tcc Ser	act Thr	ccc Pro	aaa Lys 135	496
aca Thr	aat Asn	aat Asn	gac Asp	att Ile 140	tta Leu	tct Ser	tct Ser	tgt Cys	gag Glu 145	ata Ile	aaa Lys	act Thr	gga Gly	tac Tyr 150	aac Asn	544
aaa Lys	aca Thr	gta Val	cag Gln 155	att Ile	cca Pro	att Ile	act Thr	tca Ser 160	gaa Glu	aac Asn	agt Ser	act Thr	gtg Val 165	ggt Gly	ttg Leu	592
tct Ser	aat Asn	aca Thr 170	ggc	tct Ser	aaa Lys	tta Leu	tct Ser 175	tgg Trp	tat Tyr	tca Ser	gcc Ala	cac His 180	aaa Lys	gga Gly	aca Thr	640
aca Thr	cca Pro 185	agc Ser	cct Pro	gag Glu	aca Thr	gca Ala 190	agt Ser	aca Thr	agc Ser	aga Arg	ctc Leu 195	aaa Lys	agg Arg	gac Asp	agt Ser	688
gtc Val 200	ttt Phe	tgg Trp	aga Arg	ttt Phe	tgt Cys 205	cca Pro	ggt Gly	tgc Cys	cag Gln	aaa Lys 210	ctt Leu	gtt Val	ttg Leu	ctt Leu	gca Ala 215	736
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30

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gtt Val	gaa Glu	gaa Glu	ata Ile 55	gtt Val	gtg Val	aag Lys	aac Asn	act Thr 60	cat His	ttt Phe	ctt Leu	atg Met	tgg Trp 65	gat Asp	att Ile	307
ggt Gly	ggt Gly	cag Gln 70	gag Glu	tct Ser	ctg Leu	cga Arg	tca Ser 75	tcc Ser	tgg Trp	aac Asn	aca Thr	tat Tyr 80	tac Tyr	tca Ser	aat Asn	355
aca Thr	gag Glu 85	ttc Phe	atc Ile	att Ile	ctt Leu	gtt Val 90	gtt Val	gat Asp	agc Ser	att Ile	gac Asp 95	agg Arg	gaa Glu	cga Arg	cta Leu	403
gct Ala 100	att Ile	aca Thr	aaa Lys	gaa Glu	gaa Glu 105	tta Leu	tac Tyr	aga Arg	atg Met	ttg Leu 110	gct Ala	cat His	gag Glu	gat Asp	tta Leu 115	451
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gcc Ala 15		_	_	_			_			_	_	-				395
cca Pro																443
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									cag Gln							779
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	_							_	ctc Leu				_		_	875
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		tgc Cys 465														1739
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		gac Asp														1835
		gac Asp														1883
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		ccc Pro	_	_						_			_		_	2027
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		gca Ala 625														2219
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	gcc Ala					Asp					Asn					3659
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aac tgc cag agc tg Asn Cys Gln Ser Cy 1280	t aac tgc aca ccc s Asn Cys Thr Pro 1285	agt ggc atc cag tgc gct Ser Gly Ile Gln Cys Ala 1290	cac 4187
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	r Asn Thr Thr Asp	ggg ctt ggc gcc tgc ttg Gly Leu Gly Ala Cys Leu .320	Ile
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cct gga act cca gc Pro Gly Thr Pro Ala 1345	c aca acg cca ttc a Thr Thr Pro Phe 1350	acc ttc acc acc gcc tgg Thr Phe Thr Thr Ala Trp 1355	ggtc 4379 Val
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<210> 91 <211> 5735 <212> DNA <213> Homo sapiens

<220> <221> CDS

<222> (13)..(3903)

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tcc Ser 45	ctc Leu	cta Leu	acg Thr	acg Thr	ttc Phe 50	cca Pro	Gly 999	acg Thr	tat Tyr	tca Ser 55	ttt Phe	tcc Ser	tct Ser	tcc Ser	atg Met 60	192
	_	_		_	gjå aaa					_						240
		_		_	aca Thr					_	_				_	288
					tca Ser											336
					act Thr											384
					act Thr 130					_			_		_	432
					ctc Leu			_	_							480
					ccc Pro							_			_	528
					gcc Ala			_	_							576
					cct Pro											624
					cct Pro 210											672 !
					aca Thr											720

				225					230					235		
		agc Ser														. 768
	_	aca Thr 255					_	_								816
	_	gtc Val				_		-							_	864
		acc Thr			-					-			_			912
		acc Thr	_				_	_					_			960
		ccc Pro														1008
		act Thr 335		_	_	_									_	1056
		tca Ser										_	_		_	1104
		tca Ser				_		_	_		-					1152
_		cct Pro					_	_			_					1200
_	_	atg Met			_				_		_					1248
		gtg Val 415														1296
		tta Leu														1344
		gag Glu														1392
		gct Ala	_			_	_	_				_				1440

	tcc Ser															1488
	gtt Val															1536
	aca Thr 510															1584
gca Ala 525	atg Met	act Thr	tct Ser	act Thr	acc Thr 530	cga Arg	ctc Leu	act Thr	tct Ser	gca Ala 535	atc Ile	act Thr	tcc Ser	aag Lys	act Thr 540	1632
	ttg Leu			_	_			-					_		_	1680
	tta Leu															1728
	aca Thr															1776
	ttg Leu 590															1824
	gag Glu															1872
_	acc Thr	_						_	_				_		_	1920
	act Thr													_		1968
	acg Thr															2016
	tcc Ser 670					_										2064
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	gcg Ala															2160

atc Ile	ccg Pro	acc Thr	aca Thr 720	agc Ser	cta Leu	cga Arg	act Thr	ctc Leu 725	acc Thr	cct Pro	tcg Ser	tct Ser	gtg Val 730	ggc Gly	acc Thr	2208
	act Thr															2256
atc Ile	agt Ser 750	acc Thr	tta Leu	cca Pro	act Thr	cga Arg 755	aca Thr	cac His	atc Ile	att Ile	tca Ser 760	tct Ser	tct Ser	ccc Pro	tcc Ser	2304
atc Ile 765	caa Gln	agt Ser	aca Thr	gaa Glu	acc Thr 770	tca Ser	tcc Ser	ctt Leu	gtg Val	ggc Gly 775	acc Thr	acc Thr	tct Ser	ccc Pro	acc Thr 780	2352
	tcc Ser															2400
	tcc Ser															2448
	cct Pro		_	_	_										_	2496
	act Thr 830															2544
	act Thr															2592
	gtt Val															2640
	act Thr															2688
aca Thr	gaa Glu	tct Ser 895	ttc Phe	act Thr	agg Arg	gga Gly	agt Ser 900	acg Thr	tct Ser	aca Thr	aat Asn	gca Ala 905	atc Ile	ttg Leu	act Thr	2736
tct Ser	ttt Phe 910	agt Ser	acc Thr	atc Ile	atc Ile	tgg Trp 915	tcc Ser	tca Ser	aca Thr	ccc Pro	act Thr 920	att Ile	atc Ile	atg Met	tcc Ser	2784
tct Ser 925	tct Ser	cca Pro	tct Ser	tct Ser	gcc Ala 930	agc Ser	ata Ile	act Thr	cca Pro	gtg Val 935	ttc Phe	tcc Ser	act Thr	acc Thr	att Ile 940	2832
cat His	tct Ser	gtt Val	cct Pro	tct Ser 945	tca Ser	cca Pro	tac Tyr	att Ile	ttc Phe 950	agt Ser	aca Thr	gaa Glu	aat Asn	gtg Val 955	ggc	2880
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	Ser	Ile 960	Thr	Gly	Phe	Pro	Ser 965	Leu	Ser	Ser	Ser	Ala 970	Thr	Thr	
agc act Ser Thr															2976
acc ccc Thr Pro 990									Thr						3024
act ata Thr Ile 1005			Thr					Ser					Cys		3072
gaa atg Glu Met		Pro					Thr					Thr			3120
aca gtc Thr Val	Phe					Glu					Pro				3168
agt atc Ser Ile					Thr					Thr					3216
cca gaa Pro Glu 1070	Ser			Ser					Ala						3264
act ggg Thr Gly		_					_			-		-			3312
1085	****	vai		1090	ASII	Tnr	Val		Thr 1095	Ser	Thr	Arg		Pro 1100	
_	gag	acc Thr	tgg	ctg	agc	aac	agt Ser	tct	gtg	atc	ccc	cta Leu	cct	1100 ctt	3360
1085 acc agt	gag Glu gtc Val	acc Thr J	tgg Trp 1105 acc	ctg Leu atc	agc Ser	aac Asn ctc Leu	agt Ser	tct Ser L110 atg	gtg Val aaa	atc Ile cca	ccc Pro agc Ser	cta Leu	cct Pro 1115 agc	ctt Leu ctc	3360 3408
acc agt Thr Ser	gag Glu gtc Val	acc Thr tct Ser 120	tgg Trp 1105 acc Thr	ctg Leu atc Ile	agc Ser ccg Pro	aac Asn ctc Leu	agt Ser acc Thr 1125	tct Ser L110 atg Met	gtg Val aaa Lys	atc Ile cca Pro	ccc Pro agc Ser	cta Leu agt Ser 1130	cct Pro 1115 agc Ser	ctt Leu ctc Leu	
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acc act Thr Thr acc act Thr Thr acc act Thr Thr liso acc ctt	gag Glu gtc Val atc Ile 1135 agg Arg	acc Thr tct Ser 120 ctg Leu act Thr tca Ser ttg Leu	tgg Trp 105 acc Thr agg Arg tca Ser cgc Arg	atc Ile act Thr gag Glu agg Arg 1170 acc	agc Ser ccg Pro tca Ser aca Thr 1155 aca Thr	aac Asn ctc Leu agc Ser 1140 cca Pro act Thr	agt Ser acc Thr 1125 aag Lys gtg Val cgc Arg	tct Ser 1110 atg Met tca Ser gcc Ala atc	gtg Val aaa Lys aca Thr act Thr 1175	atc Ile cca Pro cac His acc Thr 1160 tct Ser gac	ccc Pro agc Ser cca Pro 1145 cag Gln cag	agt Ser 1130 tcc Ser act Thr atg Met	cct Pro 1115 agc Ser cca Pro cct Pro	ctt Leu ctc Leu ccc Pro acc Thr aca Thr 1180 acc	3408 3456 3504

1200 1205 1210 tgt cag ctc cag acc aga tgc cag aat ggg ggt cag tgg gat ggc ctc 3696 Cys Gln Leu Gln Thr Arg Cys Gln Asn Gly Gly Gln Trp Asp Gly Leu 1220 aaa tgc cag tgc ccc agc acc ttc tat ggt tcc agt tgt gag ttt gct 3744 Lys Cys Gln Cys Pro Ser Thr Phe Tyr Gly Ser Ser Cys Glu Phe Ala 1235 1240 gtg gaa cag gtg gat cta gat gca gaa gat ttt tgc aga cat gca ggg 3792 Val Glu Gln Val Asp Leu Asp Ala Glu Asp Phe Cys Arg His Ala Gly 1250 ctt cac ctt caa ggg tgt gga gat cct gtc cct gag gaa tgg cag cat 3840 Leu His Leu Gln Gly Cys Gly Asp Pro Val Pro Glu Glu Trp Gln His 1265 cgt ggt gga cta cct ggt cct gct gga gat gcc ctt cag ccc cca gct 3888 Arg Gly Gly Leu Pro Gly Pro Ala Gly Asp Ala Leu Gln Pro Pro Ala 1285 gga gag cga gta tga gcaggtgaag accacgctga aggaggggct gcagaacgcc 3943 Gly Glu Arg Val 1295 agecaggatg tgaacagetg ccaggactec cagaccetgt gttttaagec tgactecate 4003 aaggtgaaca acaacagcaa gacagagetg acceeggeag ceatetgeeg egegeegete 4063 ccacgggcta tgaagagttc tacttcccct tggtggaggc cacccggctc cgctgtgtca 4123 ccaaatgcac gtctggggtg gacaacgcca tcgactgtca ccagggccag tgcgttctgg 4183 agacgagcgg tcccacgtgt cgctgctact ccaccgacac gcactggttc tctggcccgc 4243 gctgcgaggt ggccgtccac tggagggcgc tggtcggggc ctgacggccg gcgcgcgctg 4303 ctggtgctgc tgctcgtggc gctgggcgtc cgggcggtgc gctccggatg gtggggggc 4363 cagegeegag geeggteetg ggaccaggac aggaaatggt tegagacetg ggatgaggaa 4423 gtcgtgggca ctttttcaaa ctggggtttc gaggacgacg gaacagacaa ggatacaaat 4483 ttctatgtgg ccttggagaa cgtgacacca ctatgaaggt gcacatcaag agacccgaga 4543 tgacctcgtc ctcagtgtga gcctgcgggg ccccttcacc acccctccg ccctgccccg 4603 gacacaaggg tctgcattgc gtccatttca agaggtgacc ccaggacgcg ggcagcccag 4663 gctcctgctg ttcttgggca agatgagact gttcccccaa atcccatcct tctccttcca 4723 acttggctga aacccacctg gagacgcagt tcacgtccag gctcttccac tgtggaatct 4783 tgggcaagtc agtaacgagc ctcagtttcc tcacctgcaa aacgggtaca gcattcctgt 4843 atgatacgtc acgccgttgt tgtgaaaacc acatagactt ggtcaattct cggtcctact 4903 ctgccctccc gtctcagccc tcgtgttgcc attgcctctc tcggatcctc caatcctcac 4963 gtccttcacc tggtctctgg ccctggttct tattttctct caattcccta ctgcctgttt 5023

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<213> Homo sapiens

<220>

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ttgttgtggt tcccaggcgg tgccttcgag actggctcag cctccatctt cgatgggtcc 180
tccctggctg cctatgagga c atg ctg gtt gtg atc gtc cag tac cgg ctg
Met Leu Val Val Ile Val Gln Tyr Arg Leu
1 5 10

60

gga ata ttt ggc ttc ttc acc aca tgg gat cag cac gct ccc ggg aac

Gly Ile Phe Gly Phe Phe Thr Thr Trp Asp Gln His Ala Pro Gly Asn

15 20 25

tgg gcc ttc aag gac cag gtg gct gct cta tcc tgg gtc cag aag aac 327
Trp Ala Phe Lys Asp Gln Val Ala Ala Leu Ser Trp Val Gln Lys Asn
30 40

atc gag ttc ttc ggt ggg gac ccc agc tct gtg acc atc ttt gat tct

Ile Glu Phe Phe Gly Gly Asp Pro Ser Ser Val Thr Ile Phe Asp Ser

45 50 55

gtc tcc cat ggc cga agg ctt att cca caa agc cgt cat gga gag tgg 423

Val Ser His Gly Arg Arg Leu Ile Pro Gln Ser Arg His Gly Glu Trp ggt ggc cat cat cct tta cct gaa ggc cca tga ttatgaga agagtgagga 474 Gly Gly His His Pro Leu Pro Glu Gly Pro 75 80 534 aggcacette teaceatgtg ceatetatee caegatattt gteatetgte tettaattat 594 ctactacaga gtgaggccct agagaccagg atctctctgt ccttcaggcc cccagcataa 654 taagtggtat atatcaggca gctataaatg ttctggatga atgagctaat gaatgagctg 714

748

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<222> (901)..(1524)

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WO 02/44340 PCT/US01/47004

Met Tyr Val Leu Arg Met Ser Val Cys Ala Val Cys Ala Cys Val Cys

M	et 1	Tyr	Val	Leu	Arg 5	Met	Ser	Val	Cys	Ala 10	Val	Cys	Ala	Cys	Val 15	Cys	
				gtg Val 20	_	_			_	_	_				_		996
				tgt Cys													1044
				tgt Cys													1092
V		_		tcg Ser	_		_	-	_	_		_	_	_	-	_	1140
				tgt Cys													1188
				tgt Cys 100													1236
_	_	-	_	gtg Val	-		_	_		-	_	_				-	1284
		-		tgc Cys	_		_		_		_		_	_		_	1332
L	_	_	_	gtg Val	-	_	_		_		_		_		_		1380
				gtg Val													1428
				tat Tyr 180													1476
				tgc Cys												taa	1524
a	gta	atgag	gtg (cttt	ttag	ga t	gggaa	attga	a gat	gta	agat	ttg	3999 ¹	tga g	gggt	egtgcc	1584
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a	tg	geggt	tag (cago	gacg	tg c	ccac	ctgt	g ati	ttct	3 999	tcc	ttct	ttt (ctct	tgctg	1824

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<210> 94 <211> 254 <212> PRT <213> Homo sapiens

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<210> 95 <211> 353 <212> PRT <213> Homo sapiens

40 Gly Pro Val Cys Lys Gly Lys Trp Lys Asn Lys Glu Arg Ile Leu Ile Phe Ser Ser Arg Gly Ile Asn Phe Arg Thr Arg His Leu Met Gln Asp 70 Leu Arg Met Leu Met Pro His Ser Lys Ala Asp Thr Lys Met Asp Arg 85 90 Lys Asp Lys Leu Phe Val Ile Asn Glu Val Cys Glu Met Lys Asn Cys 105 Asn Lys Cys Ile Tyr Phe Glu Ala Lys Lys Lys Gln Asp Leu Tyr Met 115 120 Trp Leu Ser Asn Ser Pro His Gly Pro Ser Ala Lys Phe Leu Val Gln 135 140 Asn Ile His Thr Leu Ala Glu Leu Lys Met Thr Gly Asn Cys Leu Lys 150 155 Gly Ser Arg Pro Leu Leu Ser Phe Asp Pro Ala Phe Asp Glu Leu Pro 170 His Tyr Ala Leu Leu Lys Glu Leu Leu Ile Gln Ile Phe Ser Thr Pro 185 Arg Tyr His Pro Lys Ser Gln Pro Phe Val Asp His Val Phe Thr Phe 200 205 Thr Ile Leu Asp Asn Arg Ile Trp Phe Arg Asn Phe Gln Ile Ile Glu 215 220 Glu Asp Ala Ala Leu Val Glu Ile Gly Pro Arg Phe Val Leu Asn Leu 230 235 Ile Lys Ile Phe Gln Gly Ser Phe Gly Gly Pro Thr Leu Tyr Glu Asn 245 250. Pro His Tyr Gln Ser Pro Asn Met His Arg Arg Val Ile Arg Ser Ile 265 270 Thr Ala Ala Lys Tyr Arg Glu Lys Gln Gln Val Lys Asp Val Gln Lys 280 Leu Arg Lys Lys Glu Pro Lys Thr Leu Leu Pro His Asp Pro Thr Ala 295 300 Asp Val Phe Val Thr Pro Ala Glu Glu Lys Pro Ile Glu Ile Gln Trp 310 315 Val Lys Pro Glu Pro Lys Val Asp Leu Lys Ala Arg Lys Lys Arg Ile 325 330 Tyr Lys Arg Gln Arg Lys Met Lys Gln Arg Met Asp Ser Gly Lys Thr 345 Lys

<210> 96 <211> 410 <212> PRT <213> Homo sapiens

Phe Tyr Glu Asp Gly Gly Asp Glu Asp Ile Val Thr Ile Ser Gln Ala 85 90 Thr Pro Ser Ser Val Ser Arg Gly Thr Ala Pro Ser Asp Asn Arg Val 105 Thr Ser Phe Arg Asp Leu Ile His Asp Gln Asp Glu Asp Glu Glu Glu .115 120 Glu Glu Gly Gln Arg Phe Tyr Ala Gly Gly Ser Glu Arg Ser Gly Gln 140 Gln Ile Val Gly Pro Pro Arg Lys Lys Ser Pro Asn Glu Leu Val Asp 150 Asp Leu Phe Lys Gly Ala Lys Glu His Gly Ala Val Ala Val Glu Arg 170 Val Thr Lys Ser Pro Gly Glu Thr Ser Lys Pro Arg Pro Phe Ala Gly 185 Gly Gly Tyr Arg Leu Gly Ala Ala Pro Glu Glu Glu Ser Ala Tyr Val 195 200 Ala Gly Glu Lys Arg Gln His Ser Ser Gln Asp Val His Val Val Leu 215 220 Lys Leu Trp Lys Ser Gly Phe Ser Leu Asp Asn Gly Glu Leu Arg Ser 230 235 Tyr Gln Asp Pro Ser Asn Ala Gln Phe Leu Glu Ser Ile Arg Arg Gly 245 Glu Val Pro Ala Glu Leu Arg Arg Leu Ala His Gly Gly Gln Val Asn 265 Leu Asp Met Glu Asp His Arg Asp Glu Asp Phe Val Lys Pro Lys Gly 280 Ala Leu Gln Ala Phe Thr Gly Glu Gly Gln Lys Leu Gly Ser Thr Ala 295 300 Pro Gln Val Leu Ser Thr Ser Ser Pro Ala Gln Gln Ala Glu Asn Glu 310 Ala Lys Ala Ser Ser Ser Ile Leu Ile Asn Glu Ser Glu Pro Thr Thr 325 330 Asn Ile Gln Ile Arg Leu Ala Asp Gly Gly Arg Leu Val Gln Lys Phe 345 Asn His Ser His Arg Ile Ser Asp Ile Arg Leu Phe Ile Val Asp Ala 355 360 Arg Pro Ala Met Ala Ala Thr Ser Phe Ile Leu Met Thr Thr Phe Pro 375 380 Asn Lys Glu Leu Ala Asp Glu Ser Gln Thr Leu Lys Glu Ala Asn Leu 390 395 Leu Asn Ala Val Ile Val Gln Arg Leu Thr 405

<210> 97

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<212> PRT

<213> Homo sapiens

<400> 97

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 Ala
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 Pro
 Pro

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 10
 15
 15

 Cys
 Phe
 Leu
 Leu
 Leu
 Val
 Leu
 Val
 Pro
 Ser
 Asp
 Ala
 Ser
 Gly

 Gln
 Ser
 Ser
 Arg
 Asn
 Asp
 Trp
 Gln
 Val
 Leu
 Gln
 Pro
 Glu
 Gly
 Pro
 Met

 Leu
 Val
 Ala
 Gly
 Gly
 Thr
 Leu
 Leu
 Leu
 Arg
 Cys
 Met
 Val
 Gly

 Ser
 Cys
 Thr
 Asp
 Gly
 Met
 Ile
 Lys
 Trp
 Val
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 Ala
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 Ala
 Leu
 Ala
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 Ala
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 Ala
 Leu
 Ala
 Leu</t

70 75 Phe Tyr Glu Asp Gly Gly Asp Glu Asp Ile Val Thr Ile Ser Gln Ala Thr Pro Ser Ser Val Ser Arg Gly Thr Ala Pro Ser Asp Asn Arg Val 105 Thr Ser Phe Arg Asp Leu Ile His Asp Gln Asp Glu Asp Glu Glu Glu 120 115 125 Glu Glu Gly Gln Arg Phe Tyr Ala Gly Gly Ser Glu Arg Ser Gly Gln 135 140 Gln Ile Val Gly Pro Pro Arg Lys Lys Ser Pro Asn Glu Leu Val Asp 150 155 Asp Leu Phe Lys Gly Ala Lys Glu His Gly Ala Val Ala Val Glu Arg 170 Val Thr Lys Ser Pro Gly Glu Thr Ser Lys Pro Arg Val His Val Val 185 180 Leu Lys Leu Trp Lys Ser Gly Phe Ser Leu Asp Asn Gly Glu Leu Arg 200 205 Ser Tyr Gln Asp Pro Ser Asn Ala Gln Phe Leu Glu Ser Ile Arg Arg Gly Glu Val Pro Ala Glu Leu Arg Arg Leu Ala His Gly Gly Gln Val 230 235 Asn Leu Asp Met Glu Asp His Arg Asp Glu Asp Phe Val Lys Pro Lys 250 245 Gly Ala Phe Lys Ala Phe Thr Gly Glu Gly Gln Lys Leu Gly Ser Thr 265 Ala Pro Gln Val Leu Ser Thr Ser Ser Pro Ala Gln Gln Ala Glu Asn 280 285 Glu Ala Lys Ala Ser Ser Ser Ile Leu Ile Asp Glu Ser Glu Pro Thr 295 300 Thr Asn Ile Gln Ile Arg Leu Ala Asp Gly Gly Arg Leu Val Gln Lys 310 315 Phe Asn His Ser His Arg Ile Ser Asp Ile Arg Leu Phe Ile Val Asp 325 330 Ala Arg Pro Ala Met Ala Ala Thr Ser Phe Ile Leu Met Thr Thr Phe 345 Pro Asn Lys Glu Leu Ala Asp Glu Ser Gln Thr Leu Lys Glu Ala Asn 360 Leu Leu Asn Ala Val Ile Val Gln Arg Leu Thr 375

<210> 98 <211> 196 <212> PRT <213> Homo sapiens

Tyr Ala Gly Gly Ser Glu Arg Ser Gly Gln Gln Ile Val Gly Pro Pro 100 105 Arg Lys Lys Ser Pro Asn Glu Leu Val Asp Asp Leu Phe Lys Gly Ala 120 Lys Glu His Gly Ala Val Ala Val Glu Arg Val Thr Lys Ser Pro Gly 135 Glu Thr Ser Lys Pro Arg Pro Phe Ala Gly Gly Gly Tyr Arg Leu Gly 150 155 Ala Ser Thr Arg Gly Arg Val Cys Leu Cys Gly Arg Arg Lys Glu Ala 170 Ala Phe Gln Pro Arg Cys Ser Cys Ser Ile Glu Thr Leu Glu Glu Trp 185 Ile Gln Pro Gly 195

<210> 99
<211> 100
<212> PRT
<213> Homo sapiens

<400> 99 Met Phe Ala Pro Arg Leu Leu Asp Leu Gln Lys Thr Lys Tyr Ala Arg 10 Phe Met Asn His Arg Val Pro Ala His Lys Arg Tyr Gln Pro Thr Glu 20 25 Tyr Glu His Ala Ala Asn Cys Ala Thr His Ala Phe Trp Ile Ile Pro 40 Ser Ile Leu Gly Ser Ser Asn Leu Tyr Phe Leu Ser Asp Asp Asp Trp 55 Glu Thr Ile Ser Ala Trp Ile Tyr Gly Leu Gly Leu Cys Gly Leu Phe 75 70 Val Val Ser Thr Val Phe His Thr Ile Ser Trp Lys Lys Ser His Leu Arg Trp Gly Phe 100

<210> 100 <211> 580 <212> PRT <213> Homo sapiens

			100					105					110		
Gln	Pro	Gly 115		Arg	Met	Met	Leu 120	_	Leu	Pro	Arg	Leu 125	Pro	Glu	Trp
Trp	Leu 130	Val	Ser	Val	Ala	Cys 135	Met	Arg	Thr	Gly	Thr 140	Val	Met	Ile	Pro
Gly 145	Val	Thr	Gln	Leu	Thr 150	Glu	Lys	Asp	Leu	Lys 155	Tyr	Arg	Leu	Gln	Ala 160
Ser	Arg	Ala	Lys	Ser 165	Ile	Ile	Thr	Ser	Asp 170	Ser	Leu	Ala	Pro	Arg 175	Val
Asp	Ala	Ile	Ser 180	Ala	Glu	Cys	Pro	Ser 185	Leu	Gln	Thr	Lys	Leu 190	Leu	Val
Ser	Asp	Ser 195	Ser	Arg	Pro	Gly	Trp 200	Leu	Asn	Phe	Arg	Glu 205	Leu	Leu	Arg
	210					215	_		_		220		Arg		
225			-		230					235			Pro		240
				245			_		250	_			Ala	255	
			260					265					Asn 270		
-		275	-		-		280	-				285	Ala	-	
	290					295					300		Asp		
305					310		_			315			Leu	-	320
				325					330				Thr	335	
			340					345					Ala 350		
	_	355			_		360					365	Glu		
	370	_	_			375					380		Asn		
385					390					395			Pro		400
_				405	_				410				Pro	415	
	_		420					425					Phe 430		
		435	_		_		440					445	Ser		
	450					455					460		Lys		
465					470					475			Ser Glu		480
_				485					490				Ile	495	
			500					505			_		510 Ser		_
		515	_				520				,	525	Lys		
_	530					535					540		Ser		
545					550					555			Arg		560
_		Gly	_	565	Ory	Ly 6	-16	0111	570		_ ₂ ,3		9	575	
514		Jay	580												

<210> 101 <211> 109 <212> PRT <213> Homo sapiens

<210> 102 <211> 156 <212> PRT <213> Homo sapiens

<400> 102 Met Gln Lys Leu Glu Leu Gly Arg Tyr Asn Glu Thr His Ala Ile Ala Lys Trp Leu Leu Glu Lys Gln Glu Leu Gly Gly Phe Arg Ser Thr 20 Gln Thr Thr Val Val Ala Leu Glu Ala Leu Thr Arg Phe Arg Glu Ala 40 Val Pro Phe Lys Gly Ile Gln Asp Leu His Val Gln Ile Arg Ala Pro 55 Lys Thr Ala Leu Asn Val Asn Trp Tyr Ile Asp His Ser Asn Ala Tyr 70 Gln Gln Arg Ser Ala Lys Phe Leu Ala Gln Asp Asp Leu Glu Ile Lys 85 90 Ala Ser Gly Asn Gly Arg Gly Thr Ile Ser Ile Leu Thr Met Tyr His 105 Lys Ser Pro Glu Ser Arg Glu Asp Asn Cys Asn Leu Tyr His Leu Asn 120 125 Ala Thr Leu His Ser Ala Leu Glu Glu Asn Lys Lys Gly Gly Glu Thr 135 Phe Arg Leu Arg Met Glu Thr Arg Phe Gln Asn Asn

<210> 103 <211> 198 <212> PRT <213> Homo sapiens

<400> 103 Met Ala Leu Arg His Leu Ala Leu Leu Ala Gly Leu Leu Val Gly Val 10 Ala Ser Lys Ser Met Glu Asn Thr Ala Gln Leu Pro Glu Cys Cys Val 20 25 Asp Val Val Gly Val Asn Ala Ser Cys Pro Gly Ala Ser Leu Cys Gly 40 Pro Gly Cys Tyr Arg Arg Trp Asn Ala Asp Gly Ser Ala Ser Cys Val 55 Arg Cys Gly Asn Gly Thr Leu Pro Ala Tyr Asn Gly Ser Glu Cys Arg 70 75 Ser Phe Ala Gly Pro Gly Ala Pro Phe Pro Met Asn Arg Ser Ser Gly 90 85 Thr Pro Gly Arg Pro His Pro Gly Ala Pro Arg Val Ala Ala Ser Leu 105 Phe Leu Gly Thr Phe Phe Ile Ser Ser Gly Leu Ile Leu Ser Val Ala 120 Gly Phe Phe Tyr Leu Lys Arg Ser Ser Lys Leu Pro Arg Ala Cys Tyr 135 140 Arg Arg Asn Lys Ala Pro Ala Leu Gln Pro Gly Glu Ala Ala Met 155 150 Ile Pro Pro Pro Gln Ser Ser Val Arg Lys Pro Arg Tyr Val Arg Arg 170 Glu Arg Pro Leu Asp Arg Ala Thr Asp Pro Ala Ala Phe Pro Gly Glu 185 Ala Arg Ile Ser Asn Val 195

<210> 104 <211> 254 <212> PRT <213> Homo sapiens

<400> 104 Met Gly Leu Ser Ile Phe Leu Leu Cys Val Leu Gly Leu Ser Gln 1 5 10 Ala Ala Thr Pro Lys Ile Phe Asn Gly Thr Glu Cys Gly Arg Asn Ser 20 Gln Pro Trp Gln Val Gly Leu Phe Glu Gly Thr Ser Leu Arg Cys Gly Gly Val Leu Ile Asp His Arg Trp Val Leu Thr Ala Ala His Cys Ser 55 Gly Ser Arg Tyr Trp Val Arg Leu Gly Glu His Ser Leu Ser Gln Leu 75 70 Asp Trp Thr Glu Gln Ile Arg His Ser Gly Phe Ser Val Thr His Pro 90 Gly Tyr Leu Gly Ala Ser Thr Ser His Glu His Asp Leu Arg Leu Leu 105 110 Arg Leu Arg Leu Pro Val Arg Val Thr Ser Ser Val Gln Pro Leu Pro 125 120 Leu Pro Asn Asp Cys Ala Thr Ala Gly Thr Glu Cys His Val Ser Gly 135 Trp Gly Ile Thr Asn His Pro Arg Asn Pro Phe Pro Asp Leu Leu Gln 150 155 Cys Leu Asn Leu Ser Ile Val Ser His Ala Thr Cys His Gly Val Tyr 170

 Pro
 Gly
 Arg
 Ile
 Thr
 Ser
 Asn
 Met
 Val
 Cys
 Ala
 Gly
 Val
 Pro
 Gly
 Igo
 Igo</th

<210> 105 <211> 404 <212> PRT <213> Homo sapiens

<400> 105 Met Ile Trp Lys Arg Ser Ala Val Leu Arg Phe Tyr Ser Val Cys Gly 10 ' 15 Leu Leu Gln Ala Ala Ala Ser Lys Asn Lys Val Lys Gly Ser Gln 20 25 Gly Gln Phe Pro Leu Thr Gln Asn Val Thr Val Val Glu Gly Gly Thr 40 Ala Ile Leu Thr Cys Arg Val Asp Gln Asn Asp Asn Thr Ser Leu Gln 55 Trp Ser Asn Pro Ala Gln Gln Thr Leu Tyr Phe Asp Asp Lys Lys Ala 70 75 Leu Arg Asp Asn Arg Ile Glu Leu Val Arg Ala Ser Trp His Glu Leu 85 90 Ser Ile Ser Val Ser Asp Val Ser Leu Ser Asp Glu Gly Gln Tyr Thr 105 Cys Ser Leu Phe Thr Met Pro Val Lys Thr Ser Lys Ala Tyr Leu Thr 120 Val Leu Gly Val Pro Glu Lys Pro Gln Ile Ser Gly Phe Ser Ser Pro 135 140 Val Met Glu Gly Asp Leu Met Gln Leu Thr Cys Lys Thr Ser Gly Ser 150 155 Lys Pro Ala Ala Asp Ile Arg Trp Phe Lys Asn Asp Lys Glu Ile Lys 165 170 Asp Val Lys Tyr Leu Lys Glu Glu Asp Ala Asn Arg Lys Thr Phe Thr 180 185 Val Ser Ser Thr Leu Asp Phe Arg Val Asp Arg Ser Asp Asp Gly Val 200 Ala Val Ile Cys Arg Val Asp His Glu Ser Leu Asn Ala Thr Pro Gln 220 Val Ala Met Gln Val Leu Glu Ile His Tyr Thr Pro Ser Val Lys Ile 230 235 Ile Pro Ser Thr Pro Phe Pro Gln Glu Gly Gln Pro Leu Ile Leu Thr 245 250 Cys Glu Ser Lys Gly Lys Pro Leu Pro Glu Pro Val Leu Trp Thr Lys 265 270 Asp Gly Gly Glu Leu Pro Asp Pro Asp Arg Met Val Val Ser Gly Arg 280 Glu Leu Asn Ile Leu Phe Leu Asn Lys Thr Asp Asn Gly Thr Tyr Arg 295 300 Cys Glu Ala Thr Asn Thr Ile Gly Gln Ser Ser Ala Glu Tyr Val Leu 310 315 Ile Val His Asp Pro Asn Ala Leu Ala Gly Gln Asn Gly Pro Asp His

<210> 106 <211> 1600 <212> PRT <213> Homo sapiens

<400> 106

Met Thr Leu Glu Gly Leu Tyr Leu Ala Arg Gly Pro Leu Ala Arg Leu 10 Leu Leu Ala Trp Ser Ala Leu Leu Cys Met Ala Gly Gly Gln Gly Arg 20 Trp Asp Gly Ala Leu Glu Ala Ala Gly Pro Gly Arg Val Arg Arg Arg 40 Gly Ser Pro Gly Ile Leu Gln Gly Cys Val Val Pro Gly Met Leu Gly 55 Asp Pro Phe Gly Val Asp Trp Ala Val Leu Gly Pro Ala Glu Tyr Pro Gly Gly Cys Pro His Gly Gln Gly Leu Thr Arg Pro Ile Ser Leu Ser 90 Pro Lys Ala Glu Cys Val Arg Leu Pro Val Pro Cys Leu Leu Leu Ser 100 105 Arg Leu Glu Asp Ile Pro Trp Gln Glu Pro Val Cys Arg Thr Arg Ala 120 Cys Gly Glu Gly Phe Cys Ser Gln Pro Asn Leu Cys Thr Cys Ala Asp 135 Gly Thr Leu Ala Pro Ser Cys Gly Val Ser Arg Gly Ser Gly Cys Ser 150 155 Val Ser Cys Met Asn Gly Gly Thr Cys Arg Gly Ala Ser Cys Leu Cys 170 165 Gln Lys Gly Tyr Thr Gly Thr Val Cys Gly Gln Pro Ile Cys Asp Arg 185 190 Gly Cys His Asn Gly Gly Arg Cys Ile Gly Pro Asn Arg Cys Ala Cys 200 Val Tyr Gly Phe Met Gly Pro Gln Cys Glu Arg Asp Tyr Arg Thr Gly 215 Pro Cys Phe Gly Gln Val Gly Pro Glu Gly Cys Gln His Gln Leu Thr 230 235 Gly Leu Val Cys Thr Lys Ala Leu Cys Cys Ala Thr Val Gly Arg Ala 245 250 Trp Gly Leu Pro Cys Glu Leu Cys Pro Ala Gln Pro His Pro Cys Arg 265 Arg Gly Phe Ile Pro Asn Ile His Thr Gly Ala Cys Gln Asp Val Asp 280

Glu Cys Gln Ala Val Pro Gly Leu Cys Gln Gly Gly Ser Cys Val Asn

Met Val Gly Ser Phe His Cys Arg Cys Pro Val Gly His Arg Leu Ser

295

246

300

315

Asp Ser Ser Ala Ala Cys Glu Asp Tyr Arg Ala Gly Ala Cys Phe Ser Val Leu Phe Gly Gly Arg Cys Ala Gly Asp Leu Ala Gly His Tyr Thr Arg Arg Gln Cys Cys Cys Asp Arg Gly Gln Val Leu Gly Ser Val Ala Arg Ser Leu Ser Cys Val Leu Leu Gly Ala Pro Val Asn Glu Phe Gln Gln Leu Cys Ala Gln Arg Leu Pro Leu Leu Pro Gly His Pro Gly Leu Phe Pro Gly Leu Leu Gly Phe Gly Ser Asn Gly Met Gly Pro Pro Leu Gly Pro Ala Arg Leu Asn Pro His Gly Ser Asp Ala Arg Gly Ile Pro Ser Leu Gly Pro Gly Asn Ser Asn Ile Gly Thr Ala Thr Leu Asn Gln Thr Ile Asp Ile Cys Arg His Phe Thr Asn Leu Cys Leu Asn Gly Arg Cys Leu Pro Thr Pro Ser Ser Tyr Arg Cys Glu Cys Asn Val Gly Tyr Thr Gln Asp Val Arg Gly Glu Cys Ile Asp Val Asp Glu Cys Thr Ser Ser Pro Cys His His Gly Asp Cys Val Asn Ile Pro Gly Thr Tyr His Cys Arg Cys Tyr Pro Gly Phe Gln Ala Thr Pro Thr Arg Gln Ala Cys Val Asp Val Asp Glu Cys Ile Val Ser Gly Gly Leu Cys His Leu Gly Arg Cys Val Asn Thr Glu Gly Ser Phe Gln Cys Val Cys Asn Ala Gly Phe Glu Leu Ser Pro Asp Gly Lys Asn Cys Val Ala Ala Ala Pro Gly Arg Gln Thr His Leu Arg Leu Gly Glu Ala Glu Gly Phe Lys Asp Asn Ser Thr Val Gln Glu Pro Tyr Pro His Ile Thr Asp Pro Gly Arg Pro Ser Gly Val Thr Leu Ala Ser Ala Leu Arg Cys Leu Arg Pro Cys Leu Ser Ser Asp Trp Ser Arg Trp Glu His Ser Pro Ile Trp Ser Pro Leu Leu Pro Glu Met Leu Trp Leu Cys Ser Ser Val His Thr Pro Thr Leu Pro Gly Arg Pro Glu Pro Leu Gly Arg Ala Val Gly Trp Cys Thr Gly Glu Ala Gln Ile Ser Pro Gly Leu Ser Gly His Pro Gly Tyr Pro Glu Ser Gly Ala Leu Leu Glu Gly Gln Ser Arg Gly Ser Pro Glu Ala Arg Ala Gly Ala Asn Arg Gly Asp His Asn Glu Cys Ala Thr Ser Thr Met Cys Val Asn Gly Val Cys Leu Asn Glu Asp Trp Gln Leu Leu Leu Pro Leu Gln Thr Arg Ala Ser Cys Trp Arg Leu Ala Ala Ile Thr Ala Leu Asp Ala Arg His Leu Arg Glu Arg His Cys Thr Asn Thr Glu Gly Ser Phe Arg Cys Gln Cys Leu Gly Gly Leu Ala Val Gly Thr Asp Gly Arg Val Cys Val Asp Thr His Val Arg Ser Thr Cys Tyr Gly Ala Ile Glu Lys Gly Ser Cys Ala Arg Pro Phe Pro Gly Thr Val Thr Lys Ser Glu

805 810 Cys Cys Cys Ala Asn Pro Asp His Gly Phe Gly Glu Pro Cys Gln Leu 820 825 Cys Pro Ala Lys Asp Ser Ala Glu Phe Gln Ala Leu Cys Ser Ser Gly 835 840 845 Leu Gly Ile Thr Thr Asp Gly Arg Asp Ile Asn Glu Cys Ala Leu Asp 855 Pro Glu Val Cys Ala Asn Gly Val Cys Glu Asn Leu Arg Gly Ser Tyr 870 875 Arg Cys Val Cys Asn Leu Gly Tyr Glu Ala Gly Ala Ser Gly Lys Asp 885 890 Cys Thr Asp Val Asp Glu Cys Ala Leu Asn Ser Leu Leu Cys Asp Asn 905 900 Gly Trp Cys Gln Asn Ser Pro Gly Ser Tyr Ser Cys Ser Cys Pro Pro 920 925 Gly Phe His Phe Trp Gln Asp Thr Glu Ile Cys Lys Asp Val Asp Glu 935 940 Cys Leu Ser Ser Pro Cys Val Ser Gly Val Cys Arg Asn Leu Ala Gly 955 945 950 Ser Tyr Thr Cys Lys Cys Gly Pro Gly Ser Arg Leu Asp Pro Ser Gly 965 970 975
Thr Phe Cys Leu Asp Ser Thr Lys Gly Thr Cys Trp Leu Lys Ile Gln 985 990 Glu Ser Arg Cys Glu Val Asn Leu Gln Gly Ala Ser Leu Arg Ser Glu 995 1000 1005 Cys Cys Ala Thr Leu Gly Ala Ala Trp Gly Ser Pro Cys Glu Arg Cys 1015 1020 Glu Ile Gly Ser Ile Leu Leu Glu Ala Ser Gln Ala Pro Met Gly Lys 1030 1035 Ala Leu His Gly Ala Gly Pro Pro Leu Gly Trp His Glu Lys Met Thr 1045 1050 1055 Pro Leu Phe Thr Leu Val Leu Pro Val Ala Asp Ser Thr Pro Glu Val 1060 1065 1070 Thr Val Arg Asn Ser Arg Val Asp Glu Cys Leu Ser Ser Pro Cys Val 1075 1080 1085 Ser Gly Val Cys Arg Asn Leu Ala Gly Ser Tyr Thr Cys Lys Cys Gly 1090 1095 1100 Pro Gly Ser Arg Leu Asp Pro Ser Gly Thr Phe Cys Leu Asp Ser Thr 1110 1115 1120 Lys Gly Thr Cys Trp Leu Lys Ile Gln Glu Ser Arg Cys Glu Val Asn 1125 1130 1135 Leu Gln Gly Ala Ser Leu Arg Ser Glu Cys Cys Ala Thr Leu Gly Ala 1140 1145 1150 Ala Trp Gly Ser Pro Cys Glu Arg Cys Glu Ile Asp Pro Ala Cys Ala 1155 1160 1165 Arg Gly Phe Ala Arg Met Thr Gly Val Thr Cys Asn Asp Val Asn Glu 1175 1180 Cys Glu Ser Phe Pro Gly Val Cys Pro Asn Gly Arg Cys Val Asn Thr 1185 1190 1195 Ala Gly Ser Phe Arg Cys Glu Cys Pro Glu Gly Leu Met Leu Asp Ala 1205 1210 Ser Gly Arg Leu Cys Val Asp Val Arg Leu Glu Pro Cys Phe Leu Arg 1225 Trp Asp Glu Asp Glu Cys Gly Val Thr Leu Pro Gly Lys Tyr Arg Met 1235 1240 1245 Asp Val Cys Cys Cys Ser Ile Gly Ala Val Trp Gly Val Glu Cys Glu 1250 1255 1260 Ala Cys Pro Asp Pro Glu Ser Leu Glu Phe Ala Ser Leu Cys Pro Arg Gly Leu Gly Phe Ala Ser Arg Asp Phe Leu Ser Gly Arg Pro Phe Tyr 1285 1290

Lys Asp Val Asn Glu Cys Lys Val Phe Pro Gly Leu Cys Thr His Gly 1300 1305 Thr Cys Arg Asn Thr Val Gly Ser Phe His Cys Ala Cys Ala Gly Gly 1315 1320 1325 Phe Ala Leu Asp Ala Gln Glu Arg Asn Cys Thr Asp Ile Asp Glu Cys 1335 1340 Arg Ile Ser Pro Asp Leu Cys Gly Gln Gly Thr Cys Val Asn Thr Pro 1345 1350 1355 Gly Ser Phe Glu Cys Glu Cys Phe Pro Gly Tyr Glu Ser Gly Phe Met 1365 1370 Leu Met Lys Asn Cys Met Asp Val Asp Glu Cys Ala Arg Asp Pro Leu 1380 1385 1390 Leu Cys Arg Gly Gly Thr Cys Thr Asn Thr Asp Gly Ser Tyr Lys Cys 1395 1400 1405 Gln Cys Pro Pro Gly His Glu Leu Thr Ala Lys Gly Thr Ala Cys Glu 1410 1415 1420 Asp Ile Asp Glu Cys Ser Leu Ser Asp Gly Leu Cys Pro His Gly Gln 1425 1430 1435 1440 Cys Val Asn Val Ile Gly Ala Phe Gln Cys Ser Cys His Ala Gly Phe 1445 1450 1455 Gln Ser Thr Pro Asp Arg Gln Gly Cys Val Asp Ile Asn Glu Cys Arg 1460 1465 1470 Val Gln Asn Gly Gly Cys Asp Val His Cys Ile Asn Thr Glu Gly Ser 1475 1480 1485 Tyr Arg Cys Ser Cys Gly Gln Gly Tyr Ser Leu Met Pro Asp Gly Arg 1495 1500 Ala Cys Ala Asp Val Asp Glu Cys Glu Glu Asn Pro Arg Val Cys Asp 1510 1515 Gln Gly His Cys Thr Asn Met Pro Gly Gly His Arg Cys Leu Cys Tyr 1525 1530 1535 Asp Gly Phe Met Ala Thr Pro Asp Met Arg Thr Cys Val Asp Val Ala 1540 1545 1550 Leu Leu Pro Pro Ala Leu Tyr Pro Gly Pro Gly His Leu Pro His Cys 1555 1560 1565 Leu Pro Gly Thr Gly Gln Ala Leu Gln Val Ser Pro Gly Leu Asp Ala 1570 1575 1580 Val Leu Trp Gly Thr Glu Pro Ala Pro Gln Leu Gly Ile Pro Gly Arg 1590 1595

<210> 107 <211> 180 <212> PRT <213> Homo sapiens

85 90 Phe Ala Thr Leu Asn Ser Leu Gln Gly Leu Phe Ile Phe Leu Phe His 105 Cys Leu Leu Asn Ser Glu Val Arg Ala Ala Phe Lys His Lys Thr Lys 115 120 Val Trp Ser Leu Thr Ser Ser Ser Ala Arg Thr Ser Asn Ala Lys Pro 135 Phe His Ser Asp Leu Met Asn Gly Thr Arg Pro Gly Met Ala Ser Thr 150 155 Lys Leu Ser Pro Trp Asp Lys Ser Ser His Ser Ala His Arg Val Asp 170 Leu Ser Ala Val 180

<210> 108 <211> 374 <212> PRT <213> Homo sapiens

<400> 108 Met Met Pro Gly Thr Ala Leu Glu Gly Val Leu Leu Ala Val Leu Leu 10 Val Gly Leu Gln Thr Ala Thr Gly Arg Leu Leu Ser Gly Gln Pro Val 20 25 Cys Arg Gly Gly Thr Gln Arg Pro Cys Tyr Lys Val Ile Tyr Phe His 40 Asp Thr Ser Arg Arg Leu Asn Phe Glu Glu Ala Lys Glu Ala Cys Arg 55 Arg Asp Gly Gln Leu Val Ser Ile Glu Ser Glu Asp Glu Gln Lys Leu Ile Glu Lys Phe Ile Glu Asn Leu Leu Pro Ser Asp Gly Asp Phe 85 90 Trp Ile Gly Leu Arg Arg Glu Glu Lys Gln Ser Asn Ser Thr Ala 105 Cys Gln Asp Leu Tyr Ala Trp Thr Asp Gly Ser Ile Ser Gln Phe Arg 115 120 Asn Trp Tyr Val Asp Glu Pro Ser Cys Gly Ser Glu Val Cys Val Val 135 140 Met Tyr His Gln Pro Ser Ala Pro Ala Gly Ile Gly Gly Pro Tyr Met 155 Phe Gln Trp Asn Asp Asp Arg Cys Asn Met Lys Asn Asn Phe Ile Cys 165 170 Lys Tyr Ser Asp Glu Lys Pro Ala Val Pro Ser Arg Glu Ala Glu Gly 185 Glu Glu Thr Glu Leu Thr Thr Pro Val Leu Pro Glu Glu Thr Gln Glu 200 205 Glu Asp Ala Lys Lys Thr Phe Lys Glu Ser Arg Glu Ala Ala Leu Asn 215 220 Leu Ala Tyr Ile Leu Ile Pro Ser Ile Pro Leu Leu Leu Leu Val 230 235 Val Thr Thr Val Val Cys Trp Val Trp Ile Cys Arg Lys Arg Lys Arg 250 Glu Gln Pro Asp Pro Ser Thr Lys Lys Gln His Thr Ile Trp Pro Ser 260 265 Pro His Gln Gly Asn Ser Pro Asp Leu Glu Val Tyr Asn Val Ile Arg 280 285 Lys Gln Ser Glu Ala Asp Leu Ala Glu Thr Arg Pro Asp Leu Lys Asn 290 300

 Ile
 Ser
 Phe
 Arg
 Val
 Cys
 Ser
 Gly
 Glu
 Ala
 Thr
 Pro
 Asp
 Asp
 Met
 Ser
 310
 315
 320
 320

 Cys
 Asp
 Tyr
 Asp
 Asn
 Met
 Ala
 Val
 Asn
 Pro
 Ser
 Glu
 Ser
 Gly
 Phe
 Val
 Ser
 Glu
 Ser
 Glu
 Ser
 Glu
 Thr
 Asn
 Asp
 Ile
 Tyr
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<210> 109 <211> 503 <212> PRT <213> Homo sapiens

<400> 109 Met Tyr Leu Val Ala Gly Asp Arg Gly Leu Ala Gly Cys Gly His Leu 10 Leu Val Ser Leu Leu Gly Leu Leu Leu Leu Ala Arg Ser Gly Thr 20 Arg Ala Leu Val Cys Leu Pro Cys Asp Glu Ser Lys Cys Glu Glu Pro 40 . 45 Arg Asn Cys Pro Gly Ser Ile Val Gln Gly Val Cys Gly Cys Cys Tyr Thr Cys Ala Ser Gln Arg Asn Glu Ser Cys Gly Gly Thr Phe Gly Ile 70 75 Tyr Gly Thr Cys Asp Arg Gly Leu Arg Cys Val Ile Arg Pro Pro Leu 85 90 Asn Gly Asp Ser Leu Thr Glu Tyr Glu Ala Gly Val Cys Glu Asp Glu 100 105 Asn Trp Thr Asp Asp Gln Leu Leu Gly Phe Lys Pro Cys Asn Glu Asn 120 115 Leu Ile Ala Gly Cys Asn Ile Ile Asn Gly Lys Cys Glu Cys Asn Thr 135 140 Ile Arg Thr Cys Ser Asn Pro Phe Glu Phe Pro Ser Gln Asp Met Cys 150 155 Leu Ser Ala Leu Lys Arg Ile Glu Glu Glu Lys Pro Asp Cys Ser Lys 165 170 Ala Arg Cys Glu Val Gln Phe Ser Pro Arg Cys Pro Glu Asp Ser Val 180 185 - 190 Leu Ile Glu Gly Tyr Ala Pro Pro Gly Glu Cys Cys Pro Leu Pro Ser 195 200 205 Arg Cys Val Cys Asn Pro Ala Gly Cys Leu Arg Lys Val Cys Gln Pro 215 220 Gly Asn Leu Asn Ile Leu Val Ser Lys Ala Ser Gly Lys Pro Gly Glu 225 . 230 235 Cys Cys Asp Leu Tyr Glu Cys Lys Pro Val Phe Gly Val Asp Cys Arg 245 250 Thr Val Glu Cys Pro Pro Val Gln Gln Thr Ala Arg Cys Pro Pro Asp 265 Ser Tyr Glu Thr Gln Val Arg Leu Thr Ala Asp Gly Cys Cys Pro Leu 280 275 285 Pro Pro Arg Cys Glu Cys Leu Ser Gly Leu Cys Gly Phe Pro Val Cys 295 300 Glu Val Gly Ser Thr Pro Arg Ile Val Ser Arg Gly Asp Gly Thr Pro 310 315 Gly Lys Cys Cys Asp Val Phe Glu Cys Val Asn Asp Thr Lys Pro Ala

330 325 Cys Val Phe Asn Asn Val Glu Tyr Tyr Asp Gly Asp Met Phe Arg Met 345 Asp Asn Cys Arg Phe Cys Arg Cys Gln Gly Gly Val Ala Ile Cys Phe 355 360 Thr Ala Gln Cys Gly Glu Ile Asn Cys Glu Arg Tyr Tyr Val Pro Glu 375 380 Gly Glu Cys Cys Pro Val Cys Glu Asp Pro Val Tyr Pro Phe Asn Asn 395 Pro Ala Gly Cys Tyr Ala Asn Gly Leu Ile Leu Ala His Gly Asp Arg 405 410 Trp Arg Glu Asp Asp Cys Thr Phe Cys Gln Cys Val Asn Gly Glu Arg 420 425 His Cys Val Ala Thr Val Cys Gly Gln Thr Cys Thr Asn Pro Val Lys 440 Val Pro Gly Glu Cys Cys Pro Val Cys Glu Glu Pro Thr Ile Ile Thr. 460 455 Val Asp Pro Pro Ala Cys Gly Glu Leu Ser Asn Cys Thr Leu Thr Gly 470 475 Lys Asp Cys Ile Asn Gly Phe Lys Arg Asp His Asn Gly Cys Arg Thr 485 490 Cys Gln Cys Ile Asn Ser Glu 500

<210> 110 <211> 123 <212> PRT <213> Homo sapiens

<400> 110 Met Trp Leu Pro Pro Ala Leu Leu Leu Ser Leu Ser Gly Cys Phe 10 Ser Ile Gln Gly Pro Glu Ser Val Arg Ala Pro Glu Gln Gly Ser Leu 25 Thr Val Gln Cys His Tyr Lys Gln Gly Trp Glu Thr Tyr Ile Lys Trp 35 40 Trp Cys Arg Gly Val Arg Trp Asp Thr Cys Lys Ile Leu Ile Glu Thr 55 Arg Gly Ser Glu Gln Gly Glu Lys Ser Asp Arg Val Ser Ile Lys Asp 70 Asn Gln Lys Asp Arg Thr Phe Thr Val Thr Met Glu Gly Leu Arg Arg 85 90 Asp Asp Ala Asp Val Tyr Trp Cys Gly Ile Glu Arg Arg Gly Pro Asp 105 Leu Gly Thr Gln Val Lys Val Ile Val Asp Pro

<210> 111 <211> 120 <212> PRT <213> Homo sapiens

400> 111
Met Ser Cys Ile Leu Gly Phe Cys Phe Pro Gly Cys Phe Ser Ile Gln
1 5 10 15

<210> 112 <211> 346 <212> PRT <213> Homo sapiens

<400> 112 Met Glu Arg Lys Phe Met Ser Leu Gln Pro Ser Ile Ser Val Ser Glu 10 Met Glu Pro Asn Gly Thr Phe Ser Asn Asn Asn Ser Arg Asn Cys Thr . 20 25 Ile Glu Asn Phe Lys Arg Glu Phe Phe Pro Ile Val Tyr Leu Ile Ile 40 Phe Phe Trp Gly Val Leu Gly Asn Gly Leu Ser Ile Tyr Val Phe Leu 60 Gln Pro Tyr Lys Lys Ser Thr Ser Val Asn Val Phe Met Leu Asn Leu 70 Ala Ile Ser Asp Leu Leu Phe Ile Ser Thr Leu Pro Phe Arg Ala Asp 85 90 Tyr Tyr Leu Arg Gly Ser Asn Trp Ile Phe Gly Asp Leu Ala Cys Arg 105 Ile Met Ser Tyr Ser Leu Tyr Val Asn Met Tyr Ser Ser Ile Tyr Phe 120 Leu Thr Val Leu Ser Val Val Arg Phe Leu Ala Met Val His Pro Phe 135 140 Arg Leu Leu His Val Thr Ser Ile Arg Ser Ala Trp Ile Leu Cys Gly 150 155 Ile Ile Trp Ile Leu Ile Met Ala Ser Ser Ile Met Leu Leu Asp Ser 165 170 Gly Ser Glu Gln Asn Gly Ser Val Thr Ser Cys Leu Glu Leu Asn Leu 185 Tyr Lys Ile Ala Lys Leu Gln Thr Met Asn Tyr Ile Ala Leu Val Val 200 205 Gly Cys Leu Leu Pro Phe Phe Thr Leu Ser Ile Cys Tyr Leu Leu Ile 215 220 Ile Arg Val Leu Leu Lys Val Glu Val Pro Glu Ser Gly Leu Arg Val 230 235 Ser His Arg Lys Ala Leu Thr Thr Ile Ile Ile Thr Leu Ile Ile Phe 245 250 Phe Leu Cys Phe Leu Pro Tyr His Thr Leu Arg Thr Val His Leu Thr 260 265 Thr Trp Lys Val Gly Leu Cys Lys Asp Arg Leu His Lys Ala Leu Val 280 285 Ile Thr Leu Ala Leu Ala Ala Ala Asn Ala Cys Phe Asn Pro Leu Leu

<210> 113 <211> 403 <212> PRT <213> Homo sapiens

<400> 113 Met Glu Thr Tyr Ala Glu Val Gly Lys Glu Gly Lys Pro Ser Cys Ala Ser Val Asp Leu Gln Gly Asp Ser Ser Leu Gln Val Glu Ile Ser Asp 20 25 Ala Val Ser Glu Arg Asp Lys Val Lys Phe Thr Val Gln Thr Lys Ser 40 Cys Leu Pro His Phe Ala Gln Thr Glu Phe Ser Val Val Arg Gln His 55 Glu Glu Phe Ile Trp Leu His Asp Ala Tyr Val Glu Asn Glu Glu Tyr 70 75 Ala Gly Leu Ile Ile Pro Pro Ala Pro Pro Arg Pro Asp Phe Glu Ala 90 Ser Arg Glu Lys Leu Gln Lys Leu Gly Glu Gly Asp Ser Ser Val Thr 105 Arg Glu Glu Phe Ala Lys Met Lys Gln Glu Leu Glu Ala Glu Tyr Leu 115 120 Ala Ile Phe Lys Lys Thr Val Ala Met His Glu Val Phe Leu Gln Arg 135 140 Leu Ala Ala His Pro Thr Leu Arg Arg Asp His Asn Phe Phe Val Phe 150 155 Leu Glu Tyr Gly Gln Asp Leu Ser Val Arg Gly Lys Asn Arg Lys Glu 165 170 175 Leu Leu Gly Gly Phe Leu Arg Asn Ile Val Lys Ser Ala Asp Glu Ala Leu Ile Thr Gly Met Ser Gly Leu Lys Glu Val Asp Asp Phe Phe Glu 200 205 His Glu Arg Thr Phe Leu Leu Glu Tyr His Thr Arg Ile Arg Asp Ala 220 215 Cys Leu Arg Ala Asp Arg Val Met Arg Ala His Lys Cys Leu Ala Asp 235 Asp Tyr Ile Pro Ile Ser Ala Ala Leu Ser Ser Leu Gly Thr Gln Glu 245 250 Val Asn Gln Leu Arg Thr Ser Phe Leu Lys Leu Ala Glu Leu Phe Glu 265 Arg Leu Arg Lys Leu Glu Gly Arg Val Ala Ser Asp Glu Asp Leu Lys 280 Leu Ser Asp Met Leu Arg Tyr Tyr Met Arg Asp Ser Gln Ala Ala Lys 295 300 Asp Leu Leu Tyr Arg Arg Leu Arg Ala Leu Ala Asp Tyr Glu Asn Ala 310 315 Asn Lys Ala Leu Asp Lys Ala Arg Thr Arg Asn Arg Glu Val Arg Pro 325 330 Ala Glu Ser His Gln Gln Leu Cys Cys Gln Arg Phe Glu Arg Leu Ser

345

<210> 114 <211> 806 <212> PRT <213> Homo sapiens

<400> 114 Met Ala Val Arg Ala Leu Lys Leu Leu Thr Thr Leu Leu Ala Val Val 5 10 Ala Ala Ser Gln Ala Glu Val Glu Ser Glu Ala Gly Trp Gly Met 20 Val Thr Pro Asp Leu Leu Phe Ala Glu Gly Thr Ala Ala Tyr Ala Arg 40 Gly Asp Trp Pro Gly Val Val Leu Ser Met Glu Arg Ala Leu Arg Ser 55 Arg Ala Ala Leu Arg Ala Leu Arg Leu Arg Cys Arg Thr Gln Cys Ala 70 75 Ala Asp Phe Pro Trp Glu Leu Asp Pro Asp Trp Ser Pro Ser Pro Ala 85 90 Gln Ala Ser Gly Ala Ala Ala Leu Arg Asp Leu Ser Phe Phe Gly Gly 100 105 Leu Leu Arg Arg Ala Ala Cys Leu Arg Arg Cys Leu Gly Pro Pro Ala 120 Ala His Ser Leu Ser Glu Glu Met Glu Leu Glu Phe Arg Lys Arg Ser 135 140 Pro Tyr Asn Tyr Leu Gln Val Ala Tyr Phe Lys Val Gln Thr Cys Leu 150 155 Glu Pro Gly Gly Arg Gly Pro Ser Gly Glu Arg Ser Val Ala Gly Asp 165 170 Leu Arg Ser Leu Gly Asp Arg Gly Ser Val Arg Arg Glu Gly Lys Val 185 Ala Ser Trp Leu Gly Ser Ser Pro Arg Ser Arg Gly Glu Leu Leu Pro 195 200 - 205 Gly Arg Arg Pro Ser Ser Pro Ser Ser His Gly Gln Met Leu Thr Pro 215 220 Lys Ile Asn Lys Leu Glu Lys Ala Val Ala Ala His Thr Phe Phe 230 235 Val Gly Asn Pro Glu His Met Glu Met Gln Gln Asn Leu Asp Tyr Tyr 245 250 Gln Thr Met Ser Gly Val Lys Glu Ala Asp Phe Lys Asp Leu Glu Thr 260 265 Gln Pro His Met Gln Glu Phe Arg Leu Gly Val Arg Leu Tyr Ser Glu 280 285 Glu Gln Pro Gln Glu Ala Val Pro His Leu Glu Ala Ala Leu Gln Glu 295 300 Tyr Phe Val Ala Tyr Glu Glu Cys Arg Ala Leu Cys Glu Gly Pro Tyr 310 315 Asp Tyr Asp Gly Tyr Asn Tyr Leu Glu Tyr Asn Ala Asp Leu Phe Gln 325 330 Ala Ile Thr Asp His Tyr Ile Gln Val Leu Asn Cys Lys Gln Asn Cys

			340	•				345					350		
Val	Thr	Glu 355	Leu	Ala	Ser	His	Pro 360	Ser	Arg	Glu	Lys	Pro 365	Phe	Glu	Asp
	370		Ser			375					380	_	_		
385			Thr		390					395					400
Phe	Pro	Asn	Asp	Glu 405	Val	Met	Asn	Gln	Asn 410	Leu	Ala	Tyr	Tyr	Ala 415	Ala
			Glu 420					425		-		_	430		
		435	Arg				440					445			
	450		Val			455					460				
465			Val		470					475			_		480
			Ala	485					490					495	
			Thr 500					505		_			510		
		515	Thr			_	520				_	525	_		
	530		Asn			535			_		540	-			
545	_		Ile		550			_		555			_		560
			Ala	565		-	-	-	570	Ū	-			575	
			Asn 580					585					590		
		595	Gln			_	600					605			_
	610		Thr			615					620				
625			Pro		630					635			_		640
			Glu	645					650					655	
			Asn 660					665					670		_
		675	Ala	_			680	-	_			685		-	
	690		Phe			695					700				
705					710					715					Gly 720
				725					730					735	Arg
			Cys 740					745					750		
		755	Asp	-			760		_			765			
	770		Glu			775					780				
785	_		Pro	_	790	WTG	GTII	GIU	oeľ	795	SEL	GTÅ	oer	GIU	800
пув	FIO	пЛя	Asp	805	neu										

<210> 115 <211> 906 <212> PRT <213> Homo sapiens

<400> 115 Met Ala Leu Glu Gln Ala Leu Gln Ala Arg Gln Gly Glu Leu Asp Val Leu Arg Ser Leu His Ala Ala Gly Leu Leu Gly Pro Ser Leu Arg 20 Asp Pro Leu Asp Ala Leu Pro Val His His Ala Ala Arg Ala Gly Lys 35 40 Leu His Cys Leu Arg Phe Leu Val Glu Glu Ala Ala Leu Pro Ala Ala 55 Ala Arg Ala Arg Asn Gly Ala Thr Pro Ala His Asp Ala Ser Ala Thr 70 75 Gly His Leu Ala Cys Leu Gln Trp Leu Leu Ser Gln Gly Gly Cys Arg 90 Val Gln Ala Phe Pro Glu Ser Leu Gly Val Arg Ala Val Ala Leu Gly 105 Leu Val Pro Val Ser Cys Arg Asp Asn Gln Asp Lys Asp Asn Ser Gly 120 125 Ala Thr Val Leu His Leu Ala Ala Arg Phe Gly His Pro Glu Val Val 135 Asn Trp Leu Leu His His Gly Gly Gly Asp Pro Thr Ala Ala Thr Asp 150 155 Met Gly Ala Leu Pro Ile His Tyr Ala Ala Ala Lys Gly Asp Phe Pro 170 Ser Leu Arg Leu Leu Val Glu His Tyr Pro Glu Gly Val Asn Ala Gln 185 Thr Lys Asn Gly Ala Thr Pro Leu Tyr Leu Ala Cys Gln Glu Gly His 200 205 Leu Glu Val Thr Gln Tyr Leu Val Gln Glu Cys Gly Ala Asp Pro His 215 220 Ala Arg Ala His Asp Gly Met Thr Pro Leu His Ala Ala Ala Gln Met 230 235 Gly His Ser Pro Val Ile Val Trp Leu Val Ser Cys Thr Asp Val Ser 250 245 Leu Ser Glu Gln Asp Lys Asp Gly Ala Thr Ala Met His Phe Ala Ala 265 Ser Arg Gly His Thr Lys Val Leu Ser Trp Leu Leu Leu His Gly Gly 280 Glu Ile Ser Ala Asp Leu Trp Gly Gly Thr Pro Leu His Asp Ala Ala 295 300 Glu Asn Gly Glu Leu Glu Cys Cys Gln Ile Leu Val Val Asn Gly Ala 310 315 Glu Leu Asp Val Arg Asp Arg Asp Gly Tyr Thr Ala Ala Asp Leu Ser 325 330 Asp Phe Asn Gly His Ser His Cys Thr Arg Tyr Leu Arg Thr Val Glu 340 345 350 Asn Leu His Arg Gly Met Val Leu Ala Leu Gly Ala Ala Glu His Ser 360 365 Lys Ala Gln Arg Pro Glu Ala Ala Gly Gly Pro Glu Asp Glu Leu Pro 375 380 Pro Ala Lys Glu Ser Leu Glu Glu Asn Glu Trp Pro Ser Arg Gly Gln 390 395 Gly Leu Val Pro Ser Ala Pro Thr Ala Val Gly Gln Ser Val Glu His 405 410

Arg Val Leu Ser Arg Asp Pro Ser Ala Glu Leu Glu Ala Lys Gln Pro

Asp Ser Gly Met Ser Ser Pro Asn Thr Thr Val Ser Val Gln Pro Leu Asn Phe Asp Leu Ser Ser Pro Thr Ser Thr Leu Ser Asn Tyr Asp Ser Cys Ser Ser Ser His Ser Ser Ile Lys Gly Gln His Pro Pro Cys Gly Leu Ser Ser Ala Arg Ala Ala Asp Ile Gln Ser Tyr Met Asp Met Leu Asn Pro Glu Leu Gly Leu Pro Arg Gly Thr Ile Gly Lys Pro Thr Pro Pro Pro Pro Pro Ser Phe Pro Pro Pro Pro Pro Pro Pro Gly Thr Gln Leu Pro Pro Pro Pro Gly Tyr Pro Ala Pro Lys Pro Pro Val Gly Pro Gln Ala Ala Asp Ile Tyr Met Gln Thr Lys Asn Lys Leu Arg His Val Glu Thr Glu Ala Leu Lys Lys Glu Leu Ser Ser Cys Asp Gly His Asp Gly Leu Arg Arg Gln Asp Ser Ser Arg Lys Pro Arg Ala Phe Ser Lys Gln Pro Ser Thr Gly Asp Tyr Tyr Arg Gln Leu Gly Arg Cys Pro Gly Glu Thr Leu Ala Ala Arg Pro Gly Met Ala His Ser Glu Glu Ala Ala Leu Leu Pro Gly Asn His Val Pro Asn Gly Cys Ala Ala Asp Pro Lys Ala Ser Arg Glu Leu Pro Leu Pro Glu Ala Ala Ser Ser Pro Pro Pro Ala Pro Pro Leu Pro Leu Glu Ser Ala Gly Pro Gly Cys Gly Gln Arg Arg Ser Ser Ser Thr Gly Ser Thr Lys Ser Phe Asn Met Met Ser Pro Thr Gly Asp Asn Ser Glu Leu Leu Ala Glu Ile Lys Ala Gly Lys Ser Leu Lys Pro Thr 715 · Pro Gln Ser Lys Gly Leu Thr Thr Val Phe Ser Gly Ile Gly Gln Pro Ala Phe Gln Pro Asp Ser Pro Leu Pro Ser Val Ser Pro Ala Leu Ser Pro Val Arg Ser Pro Thr Pro Pro Ala Ala Gly Phe Gln Pro Leu Leu Asn Gly Ser Leu Val Pro Val Pro Pro Thr Thr Pro Ala Pro Gly Val Gln Leu Asp Val Glu Ala Leu Ile Pro Thr His Asp Glu Gln Gly Arg Pro Ile Pro Glu Trp Lys Arg Gln Val Met Val Arg Lys Met Gln Leu Lys Met Gln Glu Glu Glu Gln Arg Arg Lys Glu Glu Glu Glu Glu Ala Arg Leu Ala Ser Met Pro Ala Trp Arg Arg Asp Leu Leu Arg Lys Lys Leu Glu Glu Glu Arg Glu Gln Lys Arg Lys Glu Glu Glu Arg Gln Lys Gln Glu Glu Leu Arg Arg Glu Lys Glu Gln Ser Glu Lys Leu Arg Thr Leu Gly Tyr Asp Glu Ser Lys Leu Ala Pro Trp Gln Arg Gln Val Ile Leu Lys Lys Gly Asp Ile Ala Lys Tyr

<210> 116 <211> 848 <212> PRT <213> Homo sapiens

<400> 116 Met Ala Leu Glu Gln Ala Leu Gln Ala Arg Gln Gly Glu Leu Asp Val Leu Arg Ser Leu His Ala Ala Gly Leu Leu Gly Pro Ser Leu Arg 20 Asp Pro Leu Asp Ala Leu Pro Val His His Ala Ala Arg Ala Gly Lys 40 Leu His Cys Leu Arg Phe Leu Val Glu Glu Ala Ala Leu Pro Ala Ala 55 Ala Arg Ala Arg Asn Gly Ala Thr Pro Ala His Asp Ala Ser Ala Thr Gly His Leu Ala Cys Leu Gln Trp Leu Leu Ser Gln Gly Gly Cys Arg 85 90 Val Gln Ala Phe Pro Glu Ser Leu Gly Val Arg Ala Val Ala Leu Gly 105 Leu Val Pro Val Ser Cys Arg Asp Asn Gln Asp Lys Asp Asn Ser Gly 120 Ala Thr Val Leu His Leu Ala Ala Arg Phe Gly His Pro Glu Val Val 135 Asn Trp Leu Leu His His Gly Gly Gly Asp Pro Thr Ala Ala Thr Asp 150 155 Met Gly Ala Leu Pro Ile His Tyr Ala Ala Ala Lys Gly Asp Phe Pro 165 170 Ser Leu Arg Leu Leu Val Glu His Tyr Pro Glu Gly Val Asn Ala Gln 180 185 Thr Lys Asn Gly Ala Thr Pro Leu Tyr Leu Ala Cys Gln Glu Gly His 200 Leu Glu Val Thr Gln Tyr Leu Val Gln Glu Cys Gly Ala Asp Pro His 215 220 Ala Arg Ala His Asp Gly Met Thr Pro Leu His Ala Ala Ala Gln Met 230 235 Gly His Ser Pro Val Ile Val Trp Leu Val Ser Cys Thr Asp Val Ser 250 Leu Ser Glu Gln Asp Lys Asp Gly Ala Thr Ala Met His Phe Ala Ala 265 Ser Arg Gly His Thr Lys Val Leu Ser Trp Leu Leu Leu His Gly Gly 280 Glu Ile Ser Ala Asp Leu Trp Gly Gly Thr Pro Leu His Asp Ala Ala 295 300 Glu Asn Gly Glu Leu Glu Cys Cys Gln Ile Leu Val Val Asn Gly Ala 310 315 Glu Leu Asp Val Arg Asp Arg Asp Gly Tyr Thr Ala Ala Asp Leu Ser 325 330 Asp Phe Asn Gly His Ser His Cys Thr Arg Tyr Leu Arg Thr Val Glu 345 Asn Leu Ser Val Glu His Arg Val Leu Ser Arg Asp Pro Ser Ala Glu 355 360 Leu Glu Ala Lys Gln Pro Asp Ser Gly Met Ser Ser Pro Asn Thr Thr 375 380 Val Ser Val Gln Pro Leu Asn Phe Asp Leu Ser Ser Pro Thr Ser Thr 390 395 Leu Ser Asn Tyr Asp Ser Cys Ser Ser Ser His Ser Ser Ile Lys Gly

				405					410					415	
Gln	His	Pro	Pro 420	Сув	Gly	Leu	Ser	Ser 425		Arg	Ala	Ala	Asp 430		Gln
Ser	Tyr	Met 435	Asp	Met	Leu	Asn	Pro 440	Glu	Leu	Gly	Leu	Pro 445	Arg	Gly	Thr
	Gly _. 450	_				455					460				
465	Pro				470					475				-	480
	Pro			485					490		_		-	495	
	Lys		500					505					510		
	Ser	515	_	_	_		520	_		_		525	-		
	Lys 530					535					540				
545	Gln				550					555			_		560
	Ala			565					570		_			575	
	Gly		580					585					590		
	Pro	595					600					605			
	Ala 610					615				_	620	_	_	•	
625	Arg				630		_			635					640
	Pro		_	645					650				-	655	-
	Ser		660					665	_	-			670		
	Gly	675	_				680			-		685			
	Ser 690					695					700				
705	Phe				710		_			715					720
	Pro			725					730					735	
	Asp		740	-				745	•		_	_	750		
	Arg	755					760					765		-	-
	770					775					780				
785	Asp				790	_				795	_			_	800
	Glu			805					810					815	
	Ser		820					825		-			830		
PIO	Trp	835	wrg	GIN	vaT	тте	ьеи 840	тÀг	ъÀв	стА	Asp	845	A19	гуз	Tyr

<210> 117

<211> 588 <212> PRT

<213> Homo sapiens

<400> 117 Met Leu Arg Leu Gln Ala Pro Gly Pro Ala Gly Arg Pro Arg Cys Phe Pro Leu Arg Ala Ala Arg Leu Phe Thr Arg Phe Ala Glu Ala Gly Arg 25 Ser Thr Leu Arg Leu Pro Ala His Asp Thr Pro Gly Ala Gly Ala Val Gln Leu Leu Leu Ser Asp Cys Pro Pro Asp Arg Leu Arg Arg Phe Leu 55 Arg Thr Leu Arg Leu Lys Leu Ala Ala Ala Pro Gly Pro Gly Pro Ala 75 Ser Ala Arg Ala Gln Leu Leu Gly Pro Arg Pro Arg Asp Phe Val Thr 90 Ile Ser Pro Val Gln Pro Glu Glu Arg Arg Leu Arg Ala Ala Thr Arg 105 Val Pro Asp Thr Thr Leu Val Lys Arg Pro Val Glu Pro Gln Ala Gly 120 Ala Glu Pro Ser Thr Glu Ala Pro Arg Trp Pro Leu Pro Val Lys Arg 135 Leu Ser Leu Pro Ser Thr Lys Pro Gln Leu Ser Glu Glu Gln Ala Ala 150 155 Val Leu Arg Ala Ala Leu Lys Gly Gln Ser Ile Phe Phe Thr Gly Ser 170 165 Ala Gly Thr Gly Lys Ser Tyr Leu Leu Lys Arg Ile Leu Gly Ser Leu 185 190 Pro Pro Thr Gly Thr Glu Ala Thr Ala Ser Thr Gly Val Ala Ala Cys 195 200 His Ile Gly Gly Thr Thr Leu His Ala Phe Ala Gly Ile Gly Ser Gly 215 220 Gln Ala Pro Leu Ala Gln Cys Val Ala Leu Ala Gln Arg Pro Gly Val 230 235 Arg Gln Gly Trp Leu Asn Cys Gln Arg Leu Val Ile Asp Glu Ile Ser 245 250 Met Val Glu Ala Asp Leu Phe Asp Lys Leu Glu Ala Val Ala Arg Ala 265 Val Arg Gln Gln Asn Lys Pro Phe Gly Gly Ile Gln Leu Ile Ile Cys 280 Gly Asp Phe Leu Gln Leu Pro Pro Val Thr Lys Gly Ser Gln Pro Pro 295 300 Arg Phe Cys Phe Gln Ser Lys Ser Trp Lys Arg Gly Val Pro Val Thr 310 315 Leu Glu Leu Thr Lys Gly Gly Arg Gln Ala Asn Gln Thr Phe Phe 325 330 Leu Leu Gln Ala Val Arg Leu Gly Arg Cys Ser Asp Glu Val Thr Arg 340 345 Gln Leu Gln Ala Thr Ala Ser His Lys Val Gly Arg Asp Gly Ile Val 360 Ala Thr Arg Leu Cys Thr His Gln Asp Asp Val Ala Leu Thr Asn Glu 375 Arg Arg Leu Gln Glu Leu Pro Gly Lys Val His Arg Phe Glu Ala Met 390 395 Asp Ser Asn Pro Glu Leu Ala Ser Thr Leu Asp Ala Gln Cys Pro Val 405 410 Ser Gln Leu Leu Gln Leu Lys Leu Gly Ala Gln Val Met Leu Val Lys 425 Asn Leu Ser Val Ser Arg Gly Leu Val Asn Gly Ala Arg Gly Val Val

440 Val Gly Phe Glu Ala Glu Gly Arg Gly Leu Pro Gln Val Arg Phe Leu 455 460 Cys Gly Val Thr Glu Val Ile His Ala Asp Arg Trp Thr Val Gln Ala 470 475 Thr Gly Gly Gln Leu Leu Ser Arg Gln Gln Leu Pro Leu Gln Leu Ala 490 485 Trp Ala Met Ser Ile His Lys Ser Gln Gly Met Thr Leu Asp Cys Val 505 Glu Ile Ser Leu Gly Arg Val Phe Ala Ser Gly Gln Ala Tyr Val Ala 520 Leu Ser Arg Ala Arg Ser Leu Gln Gly Leu Arg Val Leu Asp Phe Asp 535 540 Pro Met Ala Val Arg Cys Asp Pro Arg Val Leu His Phe Tyr Ala Thr 550 555 Leu Arg Arg Gly Arg Ser Leu Ser Leu Glu Ser Pro Asp Asp Asp Glu 565 570 Ala Ala Ser Asp Gln Glu Asn Met Asp Pro Ile Leu 580 585

<210> 118 <211> 526 <212> PRT <213> Homo sapiens

<400> 118 Met Leu Arg Leu Gln Ala Pro Gly Pro Ala Gly Arg Pro Arg Cys Phe 5 10 Pro Leu Arg Ala Ala Arg Leu Phe Thr Arg Phe Ala Glu Ala Gly Arg 25 Ser Thr Leu Arg Leu Pro Ala His Asp Thr Pro Gly Ala Gly Ala Val Gln Leu Leu Ser Asp Cys Pro Pro Asp Arg Leu Arg Arg Phe Leu 55 Arg Thr Leu Arg Leu Lys Leu Ala Ala Pro Gly Pro Gly Pro Ala Ser Ala Arg Ala Gln Leu Leu Gly Pro Arg Pro Arg Asp Phe Val Thr 85 90 Ile Ser Pro Val Gln Pro Glu Glu Arg Arg Leu Arg Ala Ala Thr Arg 105 Val Pro Asp Thr Thr Leu Val Lys Arg Pro Val Glu Pro Gln Ala Gly 120 Ala Glu Pro Ser Thr Glu Ala Pro Arg Trp Pro Leu Pro Val Lys Arg 135 Leu Ser Leu Pro Ser Thr Lys Pro Gln Leu Ser Glu Glu Gln Ala Ala 155 150 Val Leu Arg Ala Ala Leu Lys Gly Gln Ser Ile Phe Phe Thr Gly Ser 170 Ala Gly Thr Gly Lys Ser Tyr Leu Leu Lys Arg Ile Leu Gly Ser Leu 185 Pro Pro Thr Gly Thr Glu Ala Thr Ala Ser Thr Gly Val Ala Ala Cys 200 His Ile Gly Gly Thr Thr Leu His Ala Phe Ala Gly Ile Gly Ser Gly 215 Gln Ala Pro Leu Ala Gln Cys Val Ala Leu Ala Gln Arg Pro Gly Val 230 235 Arg Gln Gly Trp Leu Asn Cys Gln Arg Leu Val Ile Asp Glu Ile Ser 250 245

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Met Val Glu Ala Asp Leu Phe Asp Lys Leu Glu Ala Val Ala Arg Ala
                                265
Val Arg Gln Gln Asn Lys Pro Phe Gly Gly Ile Gln Leu Ile Ile Cys
                           280
Gly Asp Phe Leu Gln Leu Pro Pro Val Thr Lys Gly Ser Gln Pro Pro
                                            300
Arg Phe Cys Phe Gln Ser Ser Pro Asn Arg Cys Ser Asp Glu Val Thr
             310
Arg Gln Leu Gln Ala Thr Ala Ser His Lys Val Gly Arg Asp Gly Ile
               325
                                   330
Val Ala Thr Arg Leu Cys Thr His Gln Asp Asp Val Ala Leu Thr Asn
                               345
Glu Arg Arg Leu Gln Glu Leu Pro Gly Lys Val His Arg Phe Glu Ala
                           360
Met Asp Ser Asn Pro Glu Leu Ala Ser Thr Leu Asp Ala Gln Cys Pro
                      375
Val Ser Gln Leu Leu Gln Leu Lys Leu Gly Ala Gln Val Met Leu Val
                   390
                                       395
Lys Asn Leu Ser Val Ser Arg Gly Leu Val Asn Gly Ala Arg Gly Val
                405
                                   410
Val Val Gly Phe Glu Ala Glu Gly Arg Gly Leu Pro Gln Val Arg Phe
                               425
Leu Cys Gly Val Thr Glu Val Ile His Ala Asp Arg Trp Thr Val Gln
                           440
                                               445
Ala Thr Gly Gly Gln Leu Leu Ser Arg Gln Gln Leu Pro Leu Gln Leu
                       455
Ala Trp Ala Met Ser Ile His Lys Ser Gln Gly Leu Arg Val Leu Asp
                   470
                                       475
Phe Asp Pro Met Ala Val Arg Cys Asp Pro Arg Val Leu His Phe Tyr
               485
                                   490
Ala Thr Leu Arg Arg Gly Arg Ser Leu Ser Leu Glu Ser Pro Asp Asp
                               505
Asp Glu Ala Ala Ser Asp Gln Glu Asn Met Asp Pro Ile Leu
                           520
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<210> 119 <211> 674 <212> PRT <213> Homo 'sapiens

<400> 119 Met Gln Thr Şer Ser Ser Arg Ser Val His Leu Ser Glu Trp Gln Lys 10 Asn Tyr Phe Ala Ile Thr Ser Gly Ile Cys Thr Gly Pro Lys Ala Asp 20 25 Ala Tyr Arg Ala Gln Ile Leu Arg Ile Gln Tyr Ala Trp Ala Asn Ser 40 Glu Ile Ser Gln Val Cys Ala Thr Lys Leu Phe Lys Lys Tyr Ala Glu 55 Lys Tyr Ser Ala Ile Ile Asp Ser Asp Asn Val Glu Ser Gly Leu Asn 75 Asn Tyr Ala Glu Asn Ile Leu Thr Leu Ala Gly Ser Gln Gln Thr Asp Ser Asp Lys Trp Gln Ser Gly Leu Ser Ile Asn Asn Val Phe Lys Met 105 Ser Ser Val Gln Lys Met Met Gln Ala Gly Lys Lys Phe Lys Asp Ser 120 Leu Leu Glu Pro Ala Leu Ala Ser Val Val Ile His Lys Glu Ala Thr

140 135 Val Phe Asp Leu Pro Lys Phe Ser Val Cys Gly Ser Ser Gln Glu Ser 150 155 Asp Ser Leu Pro Asn Ser Ala His Asp Arg Asp Arg Thr Gln Asp Phe 165 170 Pro Glu Ser Asn Arg Leu Lys Leu Leu Gln Asn Ala Gln Pro Pro Met 185 Val Thr Asn Thr Ala Arg Thr Cys Pro Thr Phe Ser Ala Pro Val Gly 200 Glu Ser Ala Thr Ala Lys Phe His Val Thr Pro Leu Phe Gly Asn Val 215 220 Lys Lys Glu Asn His Ser Ser Ala Lys Glu Asn Ile Gly Leu Asn Val 230 235 Phe Leu Ser Asn Gln Ser Cys Phe Pro Ala Ala Cys Glu Asn Pro Gln 245 250 Arg Lys Ser Phe Tyr Gly Ser Gly Thr Ile Asp Ala Leu Ser Asn Pro 265 Ile Leu Asn Lys Ala Cys Ser Lys Thr Glu Asp Asn Gly Pro Lys Glu 280 -285 Asp Ser Ser Leu Pro Thr Phe Lys Thr Ala Lys Glu Gln Leu Trp Val 295 Asp Gln Gln Lys Lys Tyr His Gln Pro Gln Arg Ala Ser Gly Ser Ser 310 315 Tyr Gly Gly Val Lys Lys Ser Leu Gly Ala Ser Arg Ser Arg Gly Ile 330 Leu Gly Lys Phe Val Pro Pro Ile Pro Lys Gln Asp Gly Glu Gln 340 345 Asn Gly Gly Met Gln Cys Lys Pro Tyr Gly Ala Gly Pro Thr Glu Pro 360 Ala His Pro Val Asp Glu Arg Leu Lys Asn Leu Glu Pro Lys Met Ile 380 Glu Leu Ile Met Asn Glu Ile Met Asp His Gly Pro Pro Val Asn Trp 390 395 Glu Asp Ile Ala Gly Val Glu Phe Ala Lys Ala Thr Ile Lys Glu Ile 405 410 Val Val Trp Pro Met Leu Arg Pro Asp Ile Phe Thr Gly Leu Arg Gly 425 Pro Pro Lys Gly Ile Leu Leu Phe Gly Pro Pro Gly Thr Gly Lys Thr 435 440 Leu Ile Gly Lys Cys Ile Ala Ser Gln Ser Gly Ala Thr Phe Phe Ser 455 460 Ile Ser Ala Ser Ser Leu Thr Ser Lys Trp Val Gly Glu Gly Glu Lys 470 475 Met Val Arg Ala Leu Phe Ala Val Ala Arg Cys Gln Gln Pro Ala Val 485 490 Ile Phe Ile Asp Glu Ile Asp Ser Leu Leu Ser Gln Arg Gly Asp Gly 505 Glu His Glu Ser Ser Arg Arg Ile Lys Thr Glu Phe Leu Val Gln Leu 520 Asp Gly Ala Thr Thr Ser Ser Glu Asp Arg Ile Leu Val Val Gly Ala 535 Thr Asn Arg Pro Gln Glu Ile Asp Glu Ala Ala Arg Arg Arg Leu Val 550 555 Lys Arg Leu Tyr Ile Pro Leu Pro Glu Ala Ser Ala Arg Lys Gln Ile 570 Val Ile Asn Leu Met Ser Lys Glu Gln Cys Cys Leu Ser Glu Glu Glu 580 585 Ile Glu Gln Ile Val Gln Gln Ser Asp Ala Phe Ser Gly Ala Asp Met 600 605 Thr Gln Leu Cys Arg Glu Ala Ser Leu Gly Pro Ile Arg Ser Leu Gln

<210> 120 <211> 333 <212> PRT <213> Homo sapiens

<400> 120 Met Asn Leu Ser Leu Val Leu Ala Ala Phe Cys Leu Gly Ile Ala Ser Ala Val Pro Lys Phe Asp Gln Asn Leu Asp Thr Lys Trp Tyr Gln Trp Lys Ala Thr His Arg Arg Leu Tyr Gly Ala Asn Glu Glu Gly Trp Arg Arg Ala Val Trp Glu Lys Asn Met Lys Met Ile Glu Leu His Asn Gly Glu Tyr Ser Gln Gly Lys His Ser Phe Thr Met Ala Met Asn Ala Phe Gly Asp Met Thr Asn Glu Glu Phe Arg Gln Val Met Asn Gly Phe Gln Tyr Gln Lys His Arg Lys Gly Lys Gln Phe Gln Glu Arg Leu Leu Glu Ile Pro Thr Ser Val Asp Trp Arg Glu Lys Gly Tyr Met Thr Pro Val Lys Asp Gln Gly Gln Cys Gly Ser Cys Trp Ala Phe Ser Ala Thr Gly Ala Leu Glu Gly Gln Met Phe Trp Lys Thr Gly Lys Leu Ile Ser Leu Asn Glu Gln Asn Leu Val Asp Cys Ser Gly Pro Gln Gly Asn Glu Gly Cys Asn Gly Asp Phe Met Asp Asn Pro Phe Arg Tyr Val Gln Glu Asn Gly Gly Leu Asp Ser Glu Glu Ser Tyr Pro Tyr Glu Ala Thr Glu Glu Ser Cys Lys Tyr Asn Pro Lys Tyr Ser Val Ala Asn Asp Thr Gly Phe Val Asp Ile Pro Lys Gln Glu Lys Ala Leu Met Lys Ala Val Ala Thr Val Gly Pro Ile Ser Val Ala Ile Asp Ala Gly His Glu Ser Phe Leu Phe Tyr Lys Glu Gly Ile Tyr Phe Glu Pro Asp Cys Ser Ser Glu Asp Met Asp His Gly Val Leu Val Val Gly Tyr Gly Phe Glu Ser Thr Glu Ser Asp Asn Asn Lys Tyr Trp Leu Val Lys Asn Ser Trp Gly Glu Glu Trp Gly Met Gly Gly Tyr Val Lys Met Ala Lys Asp Arg Arg Asn His Cys Gly Ile Ala Ser Ala Ala Ser Tyr Pro Thr Val

<210> 121 <211> 794 <212> PRT <213> Homo sapiens

<400> 121 Met Leu Cys Gly Arg Trp Arg Arg Cys Arg Arg Pro Pro Glu Glu Pro 10 Pro Val Ala Ala Gln Val Ala Ala Gln Val Ala Ala Pro Val Ala Leu 20 25 Pro Ser Pro Pro Thr Pro Ser Asp Gly Gly Thr Lys Arg Pro Gly Leu 40 Arg Ala Leu Lys Lys Met Gly Leu Thr Glu Asp Glu Asp Val Arg Ala 55 60 Met Leu Arg Gly Ser Arg Leu Arg Lys Ile Arg Ser Arg Thr Trp His 75 70 Lys Glu Arg Leu Tyr Arg Leu Gln Glu Asp Gly Leu Ser Val Trp Phe 85 90 Gln Arg Arg Ile Pro Arg Ala Pro Ser Gln His Ile Phe Phe Val Gln 105 His Ile Glu Ala Val Arg Glu Gly His Gln Ser Glu Gly Leu Arg Arg 120 125 115 Phe Gly Gly Ala Phe Ala Pro Ala Arg Cys Leu Thr Ile Ala Phe Lys 135 140 Gly Arg Arg Lys Asn Leu Asp Leu Ala Ala Pro Thr Ala Glu Glu Ala 150 155 Gln Arg Trp Val Arg Gly Leu Thr Lys Leu Arg Ala Arg Leu Asp Ala 170 165 Met Ser Gln Arg Glu Arg Leu Asp His Trp Ile His Ser Tyr Leu His 185 Arg Ala Asp Ser Asn Gln Asp Ser Lys Met Ser Phe Lys Glu Ile Lys 200 205 Ser Leu Leu Arg Met Val Asn Val Asp Met Asn Asp Met Tyr Ala Tyr 215 220 Leu Leu Phe Lys Glu Cys Asp His Ser Asn Asn Asp Arg Leu Glu Gly 230 235 Ala Glu Ile Glu Glu Phe Leu Arg Arg Leu Leu Lys Arg Pro Glu Leu 245 250 Glu Glu Ile Phe His Gln Tyr Ser Gly Glu Asp Arg Val Leu Ser Ala 265 Pro Glu Leu Leu Glu Phe Leu Glu Asp Gln Gly Glu Glu Gly Ala Thr 280 Leu Ala Arg Ala Gln Gln Leu Ile Gln Thr Tyr Glu Leu Asn Glu Thr 295 300 Ala Lys Gln His Glu Leu Met Thr Leu Asp Gly Phe Met Met Tyr Leu 310 315 Leu Ser Pro Glu Gly Ala Ala Leu Asp Asn Thr His Thr Cys Val Phe 330 325 Gln Asp Met Asn Gln Pro Leu Ala His Tyr Phe Ile Ser Ser Ser His 345 350 Asn Thr Tyr Leu Thr Asp Ser Gln Ile Gly Gly Pro Ser Ser Thr Glu 365 355 360 Ala Tyr Val Arg Tyr Cys Ser Arg Gly Ala Phe Ala Gln Gly Cys Arg 380 370 375 Cys Val Glu Leu Asp Cys Trp Glu Gly Pro Gly Gly Glu Pro Val Ile 395 390 Tyr His Gly His Thr Leu Thr Ser Lys Ile Leu Phe Arg Asp Val Val

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Gln Ala Val Arg Asp His Ala Phe Thr Leu Ser Pro Tyr Pro Val Ile
            420
                               425
Leu Ser Leu Glu Asn His Cys Gly Leu Glu Gln Gln Ala Ala Met Ala
                           440
Arg His Leu Cys Thr Ile Leu Gly Asp Met Leu Val Thr Gln Ala Leu
                        455
                                           460
Asp Ser Pro Asn Pro Glu Glu Leu Pro Ser Pro Glu Gln Leu Lys Gly
                 470
                                       475
Arg Val Leu Val Lys Gly Lys Lys Leu Pro Ala Ala Arg Ser Glu Asp
               485
                                   490
Gly Arg Ala Leu Ser Asp Arg Glu Glu Glu Glu Glu Asp Asp Glu Glu
           500
                               505
Glu Glu Glu Glu Val Glu Ala Ala Ala Gln Arg Arg Leu Ala Lys Gln
                           520
Ile Ser Pro Glu Leu Ser Ala Leu Ala Val Tyr Cys His Ala Thr Arg
                      535
                                           540
Leu Arg Thr Leu His Pro Ala Pro Asn Ala Pro Gln Pro Cys Gln Val
                    550
                                       555
Ser Ser Leu Ser Glu Arg Lys Ala Lys Lys Leu Ile Arg Glu Ala Gly
                565
                                   570
Asn Ser Phe Val Arg His Asn Ala Arg Gln Leu Thr Arg Val Tyr Pro
                               585
Leu Gly Leu Arg Met Aşn Ser Ala Asn Tyr Ser Pro Gln Glu Met Trp
                           600
Asn Ser Gly Cys Gln Leu Val Ala Leu Asn Phe Gln Thr Pro Gly Tyr
                       615
                                           620
Glu Met Asp Leu Asn Ala Gly Arg Phe Leu Val Asn Gly Gln Cys Gly
                   630
                                       635
Tyr Val Leu Lys Pro Ala Cys Leu Arg Gln Pro Asp Ser Thr Phe Asp
               645
                                   650
Pro Glu Tyr Pro Gly Pro Pro Arg Thr Thr Leu Ser Ile Gln Val Leu
            660
                               665
Thr Ala Gln Gln Leu Pro Lys Leu Asn Ala Glu Lys Pro His Ser Ile
                           680
Val Asp Pro Leu Val Arg Ile Glu Ile His Gly Val Pro Ala Asp Cys
                       695
                                           700
Ala Arg Gln Glu Thr Asp Tyr Val Leu Asn Asn Gly Phe Asn Pro Arg
                   710
                                       715
Trp Gly Gln Thr Leu Gln Phe Gln Leu Arg Ala Pro Glu Leu Ala Leu
               725
                                  730
Val Arg Phe Val Val Glu Asp Tyr Asp Ala Thr Ser Pro Asn Asp Phe
                               745
Val Gly Gln Phe Thr Leu Pro Leu Ser Ser Leu Lys Gln Gly Tyr Arg
                                              765
His Ile His Leu Leu Ser Lys Asp Gly Ala Ser Leu Ser Pro Ala Thr
                       775
Leu Phe Ile Gln Ile Arg Ile Gln Arg Ser
                   790
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<210> 122 <211> 286 <212> PRT <213> Homo sapiens

<400> 122

Met Val Asp Leu Ser Val Ser Pro Asp Ser Leu Lys Pro Val Ser Leu 1 5 10 15 Thr Ser Ser Leu Val Phe Leu Met His Leu Leu Leu Leu Gln Pro Gly

20 25 Glu Pro Ser Ser Glu Val Lys Val Leu Gly Pro Glu Tyr Pro Ile Leu 40 Ala Leu Val Gly Glu Glu Val Glu Phe Pro Cys His Leu Trp Pro Gln 55 Leu Asp Ala Gln Gln Met Glu Ile Arg Trp Phe Arg Ser Gln Thr Phe Asn Val Val His Leu Tyr Gln Glu Gln Gln Glu Leu Pro Gly Arg Gln 85 90 Met Pro Ala Phe Arg Asn Arg Thr Lys Leu Val Lys Asp Asp Ile Ala 105 Tyr Gly Ser Val Val Leu Gln Leu His Ser Ile Ile Pro Ser Asp Lys 120 125 Gly Thr Tyr Gly Cys Arg Phe His Ser Asp Asn Phe Ser Gly Glu Ala 135 Leu Trp Glu Leu Glu Val Ala Gly Leu Gly Ser Asp Pro His Leu Ser 150 155 Leu Glu Gly Phe Lys Glu Gly Gly Ile Gln Leu Arg Leu Arg Ser Ser 170 Gly Trp Tyr Pro Lys Pro Lys Val Gln Trp Arg Asp His Gln Gly Gln 185 Cys Leu Pro Pro Glu Phe Glu Ala Ile Val Trp Asp Ala Gln Asp Leu 200 205 Phe Ser Leu Glu Thr Ser Val Val Val Arg Ala Gly Ala Leu Ser Asn 215 220 Val Ser Val Ser Ile Gln Asn Leu Leu Ser Gln Lys Lys Glu Leu 230 235 Val Val Gln Ile Ala Gly Gln Trp Leu Leu Ala His Thr His Leu Pro 245 250 Ser Pro His Val Tyr Ile His Ile Gly Pro Lys Ala Val Tyr Lys Glu 260 265 Thr Met Val Leu Arg Leu Ser Ala Tyr Arg Val Cys Trp Pro

<210> 123 <211> 551 <212> PRT

<213> Homo sapiens

<400> 123 Met Thr Ser Pro Gln Ala Asp Phe Cys Leu Gly Thr Ala Leu His Ser Trp Gly Leu Trp Phe Thr Glu Glu Gly Ser Pro Ser Thr Met Leu Thr 20 25 Gly Ile Ala Val Gly Ala Leu Leu Ala Leu Val Gly Val Leu 40 Ile Leu Phe Met Phe Arg Arg Leu Arg Gln Phe Arg Gln Ala Gln Pro Thr Pro Gln Tyr Arg Phe Arg Lys Arg Asp Lys Val Met Phe Tyr Gly 70 75 Arg Lys Ile Met Arg Lys Val Thr Thr Leu Pro Asn Thr Leu Val Glu 90 Asn Thr Ala Leu Pro Arg Gln Arg Ala Arg Lys Arg Thr Lys Val Leu 105 Ser Leu Ala Lys Arg Ile Leu Arg Phe Lys Lys Glu Tyr Pro Ala Leu 120 125 Gln Pro Lys Glu Pro Pro Pro Ser Leu Leu Glu Ala Asp Leu Thr Glu 135 140

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Phe Asp Val Lys Asn Ser His Leu Pro Ser Glu Val Leu Tyr Met Leu
                  150
                                     155
Lys Asn Val Arg Val Leu Gly His Phe Glu Lys Pro Leu Phe Leu Glu
               165
                                  170
Leu Cys Lys His Ile Val Phe Val Gln Leu Gln Glu Gly Glu His Val
          180
                              185
Phe Gln Pro Arg Glu Pro Asp Pro Ser Ile Cys Val Val Gln Asp Gly
                         200
Arg Leu Glu Val Cys Ile Gln Asp Thr Asp Gly Thr Glu Val Val
                      215
                                         220
Lys Glu Val Leu Ala Gly Asp Ser Val His Ser Leu Leu Ser Ile Leu
225
         230
                                     235
Asp Ile Ile Thr Gly His Ala Ala Pro Tyr Lys Thr Val Ser Val Arg
              245
                                 250
Ala Ala Ile Pro Ser Thr Ile Leu Arg Leu Pro Ala Ala Ala Phe His
                       265
Gly Val Phe Glu Lys Tyr Pro Glu Thr Leu Val Arg Val Val Gln Ile
                       280
                                            285
Ile Met Val Arg Leu Gln Arg Val Thr Phe Leu Ala Leu His Asn Tyr
                      295
Leu Gly Leu Thr Thr Glu Leu Phe Asn Ala Glu Ser Gln Ala Ile Pro
                  310
                                     315
Leu Val Ser Val Ala Ser Val Ala Ala Gly Lys Ala Lys Lys Gln Val
               325
                                 330
Phe Tyr Gly Glu Glu Arg Leu Lys Lys Pro Pro Arg Leu Gln Glu
                             345
Ser Cys Asp Ser Gly Thr Val Leu His Gln Gly Gly Gln Cys Pro Ala
                         360
Pro Glu Ser Gly Gly Ser Cys Ser His Cys Leu Arg Ser Pro Gln Val
                      375
                                        380
Ile Leu His Met Pro Glu Ala Thr Thr His Ile Pro Gly Ser Pro His
                  390
                                     395
Thr Ala Gln Val Thr Leu Gln Val Pro Gln Val Thr Ser His Ala Pro
              405
                                  410
Gln Val Tyr Ser His Ala Pro Gln Val Pro Ser Arg Ala Ser Gly Pro
          420
                             425
Leu Thr Arg Ala Pro Gly His Leu Thr Cys Pro Pro Gly Leu Ile Arg
                         440
                                          445
Trp Pro Pro Arg Ser Pro His Val Ser Pro Ser Pro His Met Arg Ala
                     455
                                        460
Gly Cys Pro Gln Thr Ser Pro Gly Leu Ile Arg Cys Ala His Leu Leu
          470
                                    475
Thr Cys Gly Leu Asp Val Leu Lys Pro Pro Thr Val Ser Leu Arg Val
              485
                        490
                                          495
Pro Val Ser Ser His Glu Ala Arg Met Ser Ser Asp Arg Pro Arg Thr
          500
                              505
Leu His Pro Pro Phe Phe Ser Cys Ser Gln Asn Ser Pro Leu Gly Gln
                         520
                                  525
Val Pro Gly Gly Glu Trp Ala Ser Arg Asp Gly Leu Ser Pro Ala Val
                      535
Leu Ser Ala Asn Arg Gly Ala
                   550
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<210> 124 <211> 328 <212> PRT <213> Homo sapiens

<400> 124 Met Ala Leu Pro Ala Leu Gly Leu Asp Pro Trp Ser Leu Leu Gly Leu 10 Phe Leu Phe Gln Leu Leu Gln Leu Leu Leu Pro Thr Thr Ala Gly 20 .25 Gly Gly Gly Gln Gly Pro Met Pro Arg Val Arg Tyr Tyr Ala Gly Asp 40 Glu Arg Arg Ala Leu Ser Phe Phe His Gln Lys Gly Leu Gln Asp Phe 55 60 Asp Thr Leu Leu Ser Gly Asp Gly Asn Thr Leu Tyr Val Gly Ala 70 Arg Glu Ala Ile Leu Ala Leu Asp Ile Gln Asp Pro Gly Val Pro Arg 85 90 Leu Lys Asn Met Ile Pro Trp Pro Ala Ser Asp Arg Lys Lys Ser Glu 100 105 110 Cys Ala Phe Lys Lys Ser Asn Glu Thr Gln Cys Phe Asn Phe Ile 120 Arg Val Leu Val Ser Tyr Asn Val Thr His Leu Tyr Thr Cys Gly Thr 135 140 Phe Ala Phe Ser Pro Ala Cys Thr Phe Ile Glu Leu Gln Asp Ser Tyr 150 155 Leu Leu Pro Ile Ser Glu Asp Lys Val Met Glu Gly Lys Gly Gln Ser 165 170 Pro Phe Asp Pro Ala His Lys His Thr Ala Val Leu Val Asp Gly Met 185 190 Leu Tyr Ser Gly Thr Met Asn Asn Phe Leu Gly Ser Glu Pro Ile Leu 195 . 200 Met Arg Thr Leu Gly Ser Gln Pro Val Leu Lys Thr Asp Asn Phe Leu 215 220 Arg Trp Leu His His Asp Ala Ser Phe Val Ala Ala Ile Pro Ser Thr 230 235 Gln Val Val Tyr Phe Phe Phe Glu Glu Thr Ala Ser Glu Phe Asp Phe 245 250 255 Phe Glu Arg Leu His Thr Ser Arg Val Ala Arg Val Cys Lys Asn Asp 265 Val Gly Gly Glu Lys Leu Leu Gln Lys Lys Trp Thr Thr Phe Leu Lys 275 280 Ala Gln Leu Leu Cys Thr Gln Pro Gly Gln Leu Pro Phe Asn Val Ile 295 300 Arg His Ala Val Leu Leu Pro Ala Asp Ser Pro Thr Ala Pro His Ile 310 315 Tyr Ala Val Phe Thr Ser Gln Trp 325

<210> 125 <211> 53 <212> PRT <213> Homo sapiens

<210> 126 <211> 110 <212> PRT <213> Homo sapiens

<210> 127 <211> 212 <212> PRT <213> Homo sapiens

<400> 127 Met Leu Ser Ser Val Val Phe Trp Gly Leu Ile Ala Leu Ile Gly Thr 10 Ser Arg Gly Ser Tyr Pro Phe Ser His Ser Met Lys Pro His Leu His 25 Pro Arg Leu Tyr His Gly Cys Tyr Gly Asp Ile Met Thr Met Lys Thr 40 Ser Gly Ala Thr Cys Asp Ala Asn Ser Val Met Asn Cys Gly Ile Arg 55 60 Gly Ser Glu Met Phe Ala Glu Met Asp Leu Arg Ala Ile Lys Pro Tyr 75 Gln Thr Leu Ile Lys Glu Val Gly Gln Arg His Cys Val Asp Pro Ala 85 90 Val Ile Ala Ala Ile Ile Ser Arg Glu Ser His Gly Gly Ser Val Leu 100 105 Gln Asp Gly Trp Asp His Arg Gly Leu Lys Phe Gly Leu Met Gln Leu 120 125 Asp Lys Gln Thr Tyr His Pro Val Gly Ala Trp Asp Ser Lys Glu His 135 140 Leu Ser Gln Ala Thr Gly Ile Leu Thr Glu Arg Ile Lys Ala Ile Gln 150 155 Lys Lys Phe Pro Thr Trp Ser Val Ala Gln His Leu Lys Gly Gly Leu 165 170 Ser Ala Phe Lys Ser Gly Ile Glu Ala Ile Ala Thr Pro Ser Asp Ile 180 185 190 Asp Asn Asp Phe Val Asn Asp Ile Ile Ala Arg Ala Lys Phe Tyr Lys 195 200 Arg Gln Ser Phe

210

<210> 128 <211> 267 <212> PRT <213> Homo sapiens

<400> 128 Met Ile Gly Asn Asn Met Ile Thr Cys Ile Asn Gly Ile Trp Thr Glu 10 Leu Pro Met Cys Val Ala Thr His Gln Leu Lys Arg Cys Lys Ile Ala 20 25 Gly Val Asn Ile Lys Thr Leu Leu Lys Leu Ser Gly Lys Glu Phe Asn 35 40 His Asn Ser Arg Ile Arg Tyr Arg Cys Ser Asp Ile Phe Arg Tyr Arg 55 60 His Ser Val Cys Ile Asn Gly Lys Trp Asn Pro Glu Val Asp Cys Thr 70 75 Glu Lys Arg Glu Gln Phe Cys Pro Pro Pro Gln Ile Pro Asn Ala · 85 90 Gln Asn Met Thr Thr Thr Val Asn Tyr Gln Asp Gly Glu Lys Val Ala 100 105 Val Leu Cys Lys Glu Asn Tyr Leu Leu Pro Glu Ala Lys Glu Ile Val 120 Cys Lys Asp Gly Arg Trp Gln Ser Leu Pro Arg Cys Val Glu Ser Thr 130 135 140 Ala Tyr Cys Gly Pro Pro Pro Ser Ile Asn Asn Gly Asp Thr Thr Ser 150 155 Phe Pro Leu Ser Val Tyr Pro Pro Gly Ser Thr Val Thr Tyr Arg Cys 170 Gln Ser Phe Tyr Lys Leu Gln Gly Ser Val Thr Val Thr Cys Arg Asn 180 185 190 Lys Gln Trp Ser Glu Pro Pro Arg Cys Leu Asp Pro Cys Val Val Ser 200 205 195 Glu Glu Asn Met Asn Lys Asn Asn Ile Gln Leu Lys Trp Arg Asn Asp 215 Gly Lys Leu Tyr Ala Lys Thr Gly Asp Ala Val Glu Phe Gln Cys Lys 230 235 Phe Pro His Lys Ala Met Ile Ser Ser Pro Pro Phe Arg Ala Ile Cys 245 250 Gln Glu Gly Lys Phe Glu Tyr Pro Ile Cys Glu 260

<210> 129 <211> 1364 <212> PRT <213> Homo sapiens

Leu Ala Ala Met Leu Val Val Pro Gln Ala Glu Thr Gln Gly Pro Val Glu Pro Ser Trp Glu Asn Ala Gly His Thr Met Asp Gly Gly Ala Pro Thr Ser Ser Pro Thr Arg Arg Val Ser Phe Val Pro Pro Val Thr Val Phe Pro Ser Leu Ser Pro Leu Asn Pro Ala His Asn Gly Arg Val Cys Ser Thr Trp Gly Asp Phe His Tyr Lys Thr Phe Asp Gly Asp Val Phe Arg Phe Pro Gly Leu Cys Asn Tyr Val Phe Ser Glu His Cys Arg Ala Ala Tyr Glu Asp Phe Asn Val Gln Leu Arg Arg Gly Leu Val Gly Ser Arg Pro Val Val Thr Arg Val Val Ile Lys Ala Gln Gly Leu Val Leu Glu Ala Ser Asn Gly Ser Val Leu Ile Asn Gly Gln Arg Glu Glu Leu Pro Tyr Ser Arg Thr Gly Leu Leu Val Glu Gln Ser Gly Asp Tyr Ile Lys Val Ser Ile Arg Leu Val Leu Thr Phe Leu Trp Asn Gly Glu Asp Ser Ala Leu Leu Glu Leu Asp Pro Lys Tyr Ala Asn Gln Thr Cys Gly Leu Cys Gly Asp Phe Asn Gly Leu Pro Ala Phe Asn Glu Phe Tyr Ala His Ser Glu Cys His Leu Asp Ala Arg Leu Thr Pro Leu Gln Phe Gly Asn Leu Gln Lys Leu Asp Gly Pro Thr Glu Gln Cys Pro Asp Pro Leu Pro Leu Pro Ala Gly Asn Cys Thr Asp Glu Glu Gly Ile Cys His Arg Thr Leu Leu Gly Pro Ala Phe Ala Glu Cys His Ala Leu Val Asp Ser Thr Ala Tyr Leu Ala Ala Cys Ala Gln Asp Leu Cys Arg Cys Pro Thr Cys Pro Cys Ala Thr Phe Val Glu Tyr Ser Arg Gln Cys Ala His Ala Gly Gly Gln Pro Arg Asn Trp Arg Cys Pro Glu Leu Cys Pro Arg Thr Cys Pro Leu Asn Met Gln His Gln Glu Cys Gly Ser Pro Cys Thr Asp Thr Cys Ser Asn Pro Gln Arg Ala Gln Leu Cys Glu Asp His Cys Val Asp Gly Cys Phe Cys Pro Pro Gly Thr Val Leu Asp Asp Ile Thr His Ser Gly Cys Leu Pro Leu Gly Gln Cys Pro Cys Thr His Gly Gly Arg Thr Tyr Ser Pro Gly Thr Ser Phe Asn Thr Thr Cys Ser Ser Cys Thr Cys Ser Gly Gly Leu Trp Gln Cys Gln Asp Leu Pro Cys Pro Gly Thr Cys Ser Val Gln Gly Gly Ala His Ile Ser Thr Tyr Asp Glu Lys Leu Tyr Asp Leu His Gly Asp Cys Ser Tyr Val Leu Ser Lys Lys Cys Ala Asp Ser Ser Phe Thr Val Leu Ala Glu Leu Arg Lys Cys Gly Leu Thr Asp Asn Glu Asn Cys Leu Lys Ala Val Thr Leu Ser Leu Asp Gly Gly Asp Thr Ala Ile Arg Val Gln Ala Asp Gly Gly Val Phe Leu Asn Ser

535 Ile Tyr Thr Gln Leu Pro Leu Ser Ala Ala Asn Ile Thr Leu Phe Thr 550 Pro Ser Ser Phe Phe Ile Val Val Gln Thr Gly Leu Gly Leu Gln Leu 570 Leu Val Gln Leu Val Pro Leu Met Gln Val Phe Val Arg Leu Asp Pro 585 580 Ala His Gln Gly Gln Met Cys Gly Leu Cys Gly Asn Phe Asn Gln Asn 600 Gln Ala Asp Asp Phe Thr Ala Leu Ser Gly Val Val Glu Ala Thr Gly 615 620 Ala Ala Phe Ala Asn Thr Trp Lys Ala Gln Ala Ala Cys Ala Asn Ala 630 Arg Asn Ser Phe Glu Asp Pro Cys Ser Leu Ser Val Glu Asn Glu Asn 645 650 Tyr Ala Arg His Trp Cys Ser Arg Leu Thr Asp Pro Asn Ser Ala Phe 665 Ser Arg Cys His Ser Ile Ile Asn Pro Lys Pro Phe His Ser Asn Cys 680 Met Phe Asp Thr Cys Asn Cys Glu Arg Ser Glu Asp Cys Leu Cys Ala 695 700 Ala Leu Ser Ser Tyr Val His Ala Cys Ala Ala Lys Gly Val Gln Leu 710 715 Ser Asp Trp Arg Asp Gly Val Cys Thr Lys Tyr Met Gln Asn Cys Pro 730 Lys Ser Gln Arg Tyr Ala Tyr Val Val Asp Ala Cys Gln Pro Thr Cys 745 Arg Gly Leu Ser Glu Ala Asp Val Thr Cys Ser Val Ser Phe Val Pro 760 Val Asp Gly Cys Thr Cys Pro Ala Gly Thr Phe Leu Asn Asp Ala Gly 775 Ala Cys Val Pro Ala Gln Lys Cys Pro Cys Tyr Ala His Gly Thr Val 790 795 Leu Ala Pro Gly Glu Val Val His Asp Glu Gly Ala Val Cys Ser Cys 805 810 Thr Gly Gly Lys Leu Ser Cys Leu Gly Ala Ser Leu Gln Lys Ser Thr 820 825 Gly Cys Ala Ala Pro Met Val Tyr Leu Asp Cys Ser Asn Ser Ser Ala 840 Gly Thr Pro Gly Ala Glu Cys Leu Arg Ser Cys His Thr Leu Asp Val 855 Gly Cys Phe Ser Thr His Cys Val Ser Gly Cys Val Cys Pro Pro Gly 875 870 Leu Val Ser Asp Gly Ser Gly Gly Cys Ile Ala Glu Glu Asp Cys Pro 890 Cys Val His Asn Glu Ala Thr Tyr Lys Pro Gly Glu Thr Ile Arg Val 905 Asp Cys Asn Thr Cys Thr Cys Arg Asn Arg Arg Trp Glu Cys Ser His 920 Arg Leu Cys Leu Gly Thr Cys Val Ala Tyr Gly Asp Gly His Phe Ile Thr Phe Asp Gly Asp Arg Tyr Ser Phe Glu Gly Ser Cys Glu Tyr Ile 950 955 Leu Ala Gln Asp Tyr Cys Gly Asp Asn Thr Thr His Gly Thr Phe Arg 965 970 Ile Val Thr Glu Asn Ile Pro Cys Gly Thr Thr Gly Thr Thr Cys Ser 985 Lys Ala Ile Lys Leu Phe Val Glu Ser Tyr Glu Leu Ile Leu Gln Glu 1000 1005 Gly Thr Phe Lys Ala Val Ala Arg Gly Pro Gly Gly Asp Pro Pro Tyr 1020 1015

Lys Ile Arg Tyr Met Gly Ile Phe Leu Val Ile Glu Thr His Gly Met 1030 1035 Ala Val Ser Trp Asp Arg Lys Thr Ser Val Phe Ile Arg Leu His Gln 1045 1050 Asp Tyr Lys Gly Arg Val Cys Gly Leu Cys Gly Asn Phe Asp Asp Asn 1065 1060 1070 Ala Ile Asn Asp Phe Ala Thr Arg Ser Arg Ser Val Val Gly Asp Ala 1075 1080 1085 Leu Glu Phe Gly Asn Ser Trp Lys Leu Ser Pro Ser Cys Pro Asp Ala 1090 . 1095 1100 Leu Ala Pro Lys Asp Pro Cys Thr Ala Asn Pro Phe Arg Lys Ser Trp 1115 1110 Ala Gln Lys Gln Cys Ser Ile Leu His Gly Pro Thr Phe Ala Ala Cys 1125 1130 1135 Arg Ser Gln Val Asp Ser Thr Lys Tyr Tyr Glu Ala Cys Val Asn Asp 1140 1145 1150 Ala Cys Ala Cys Asp Ser Gly Gly Asp Cys Glu Cys Phe Cys Thr Ala 1155 1160 1165 Val Ala Ala Tyr Ala Gln Ala Cys His Asp Ala Gly Leu Cys Val Ser 1175 1180 Trp Arg Thr Pro Asp Thr Cys Pro Leu Phe Cys Asp Phe Tyr Asn Pro 1185 1190 1195 1200 His Gly Gly Cys Glu Trp His Tyr Gln Pro Cys Gly Ala Pro Cys Leu 1205 1210 1215 Lys Thr Cys Arg Asn Pro Ser Gly His Cys Leu Val Asp Leu Pro Gly 1220 1225 1230 Leu Glu Gly Cys Tyr Pro Lys Cys Pro Pro Ser Gln Pro Phe Phe Asn 1235 1240 1245 Glu Asp Gln Met Lys Cys Val Ala Gln Cys Gly Cys Tyr Asp Lys Asp 1255 1260 Gly Asn Tyr Tyr Asp Val Gly Ala Arg Val Pro Thr Ala Glu Asn Cys 1270 1275 Gln Ser Cys Asn Cys Thr Pro Ser Gly Ile Gln Cys Ala His Ser Leu 1285 1290 1295 Glu Ala Cys Thr Cys Thr Tyr Glu Asp Arg Thr Tyr Ser Tyr Gln Asp 1300 1305 1310 Val Ile Tyr Asn Thr Thr Asp Gly Leu Gly Ala Cys Leu Ile Ala Ile 1315 1320 1325 Cys Gly Ser Asn Gly Thr Ile Ile Arg Lys Ala Val Ala Cys Pro Gly 1335 1340 Thr Pro Ala Thr Thr Pro Phe Thr Phe Thr Thr Ala Trp Val Pro His 1345 1350 1355 Ser Thr Thr Ser

<210> 130 <211> 1296 <212> PRT <213> Homo sapiens

Asp Gly Thr Thr His Thr Glu Thr Ile Thr Ser Leu Pro Ala Ser Thr Ser Thr Leu His Thr Thr Ala Glu Ser Thr Thr Ala His Thr Thr Thr Thr Ser Phe Thr Thr Ser Thr Thr Met Glu Ser Pro Ser Ser Val Ala Thr Thr Ser Thr Gly Gln Thr Thr Phe Ser Ser Ser Thr Ala Thr Phe Thr Glu Thr Thr Leu Thr Pro Thr Thr Asp Phe Ser Glu Glu Thr Leu Thr Thr Ala Met Thr Ser Thr Pro Pro Ile Thr Ser Ser Ile Thr Pro Thr Asn Thr Val Thr Ser Met Thr Thr Met Thr Ser Trp Pro Thr Ala Thr Asn Thr Leu Ser Ser Leu Thr Thr Asn Ile Leu Ser Ser Thr Pro Val Pro Ser Thr Glu Arg Thr Thr Ser His Thr Thr Asn Ile Asn Pro Val Ser Thr Leu Val Thr Thr Leu Pro Thr Thr Ile Thr Arg Ser Thr Pro Thr Ser Glu Thr Thr Tyr Pro Ile Ser Ser Thr Ser Thr Val Thr Glu Ser Thr Thr Glu Ile Thr Tyr Ser Thr Thr Met Thr Glu Thr Ser Ser Ser Ala Thr Ser Leu Pro Leu Thr Ser Pro Leu Val Ser Thr Thr Glu Thr Ala Lys Thr Pro Thr Thr Ile Leu Val Thr Thr Thr Thr Lys Thr Thr Ser His Ser Thr Thr Ser Phe Thr Ser Ser Thr Val Tyr Ser Thr Ala Ser Thr His Thr Thr Ala Ile Thr Ser Val Pro Thr Thr Leu Gly Thr Met Val Thr Ser Thr Ser Arg Ile Pro Ser Thr Val Ser Thr Ser Ile Pro Thr Ser Gln Pro Lys Thr Val Asn Ser Ser Ser Gly Gly Ile Thr Gly Ser Leu Pro Met Met Thr Asp Leu Thr Ser Gly 355 360 Tyr Thr Val Ser Ser Met Ser Ala Ile Pro Thr Thr Val Ile Pro Thr Ser Leu Thr Val Gln Asn Thr Glu Thr Ser Ile Phe Val Ser Met Thr Ser Ala Thr Thr Pro Ser Gly Arg Pro Thr Phe Thr Ser Thr Val Asn Thr Pro Thr Arg Ser Leu Leu Thr Ser Phe Pro Thr Thr His Leu Phe Ser Ser Ser Met Ser Glu Ser Ser Ala Gly Thr Thr His Thr Glu Ser Ile Ser Ser Pro Pro Ala Thr Thr Ser Thr Leu His Thr Thr Ala Glu Ser Thr Pro Ser Cys Thr Thr Thr Thr Ser Phe Ile Thr Ser Thr Thr Met Glu Pro Leu Ser Thr Ile Val Ala Thr Thr Gly Thr Val Lys Thr Thr Val Thr Ser Ser Thr Ala Thr Phe Arg Glu Thr Thr Thr Leu Thr Ser Thr Thr Asp Ile Ser Thr Glu Ser Leu Met Thr Ala Met Thr Ser Thr Thr Arg Leu Thr Ser Ala Ile Thr Ser Lys Thr Thr Leu Thr Ser

Leu Lys Thr Thr Ala Ser Arg Pro Thr Ala Asn Ser Thr Leu Ser Ser Leu Thr Ser Ser Ile Leu Ser Ser Thr Leu Val Pro Ser Thr Asp Met Ile Thr Ser His Thr Thr Asn Leu Thr Arg Ser Ser Pro Leu Leu Ala Thr Leu Pro Thr Thr Ile Thr Arg Ser Thr Pro Thr Ser Glu Thr Thr Tyr Pro Thr Ser Pro Thr Ser Thr Val Lys Gly Ser Thr Thr Ser Ile Arg Tyr Ser Thr Ser Met Thr Gly Thr Leu Ser Met Glu Thr Ser Leu Pro Pro Thr Ser Ser Ser Leu Pro Thr Thr Glu Thr Ala Thr Met Thr 645 650 Pro Thr Thr Leu Ile Thr Thr Pro Asn Thr Thr Ser His Ser Thr Pro Ser Phe Thr Ser Ser Thr Ile Tyr Ser Thr Val Ser Thr Ser Thr Thr Ala Ile Thr Ser His Phe Thr Thr Ser Glu Thr Ala Val Thr Pro Thr Pro Val Thr Pro Ser Ser Leu Ser Thr Asp Ile Pro Thr Thr Ser Leu Arg Thr Leu Thr Pro Ser Ser Val Gly Thr Ser Thr Ser Leu Thr Thr Thr Asp Phe Pro Ser Ile Pro Thr Asp Ile Ser Thr Leu Pro Thr Arg Thr His Ile Ile Ser Ser Pro Ser Ile Gln Ser Thr Glu Thr Ser Ser Leu Val Gly Thr Thr Ser Pro Thr Met Ser Thr Val Arg Met Thr Leu Arg Ile Thr Glu Asn Thr Pro Ile Ser Ser Phe Ser Thr Ser Ile Val Val Ile Pro Glu Thr Pro Thr Gln Thr Pro Pro Val Leu Thr Ser Ala Thr Gly Thr Gln Thr Ser Pro Ala Pro Thr Thr Val Thr Phe Gly Ser Thr Asp Ser Ser Thr Ser Thr Leu His Thr Leu Thr Pro Ser Thr Ala Leu Ser Thr Ile Val Ser Thr Ser Gln Val Pro Ile Pro Ser Thr His Ser Ser Thr Leu Gln Thr Thr Pro Ser Thr Pro Ser Leu Gln Thr Ser Leu Thr Ser Thr Ser Glu Phe Thr Thr Glu Ser Phe Thr Arg Gly Ser Thr Ser Thr Asn Ala Ile Leu Thr Ser Phe Ser Thr Ile Ile Trp Ser Ser Thr Pro Thr Ile Ile Met Ser Ser Pro Ser Ser Ala Ser Ile Thr Pro Val Phe Ser Thr Thr Ile His Ser Val Pro Ser Ser Pro Tyr Ile Phe Ser Thr Glu Asn Val Gly Ser Ala Ser Ile Thr Gly Phe Pro Ser Leu Ser Ser Ser Ala Thr Thr Ser Thr Ser Ser Thr Ser Ser Ser Leu Thr Thr Ala Leu Thr Glu Ile Thr Pro Phe Ser Tyr Ile Ser Leu Pro Ser Thr Thr Pro Cys Pro Gly Thr Ile Thr Ile Thr Ile Val Pro Ala Ser Pro Thr Asp Pro Cys Val Glu Met Asp Pro Ser Thr Glu Ala Thr Ser Pro Pro Thr Thr Pro Leu Thr Val Phe Pro

1030 1035 Phe Thr Thr Glu Met Val Thr Cys Pro Thr Ser Ile Ser Ile Gln Thr 1045 1050 Thr Leu Thr Thr Tyr Met Asp Thr Ser Ser Met Met Pro Glu Ser Glu 1060 1065 1070 . Ser Ser Ile Ser Pro Asn Ala Ser Ser Ser Thr Gly Thr Gly Thr Val 1075 1080 1085 Pro Thr Asn Thr Val Phe Thr Ser Thr Arg Leu Pro Thr Ser Glu Thr 1095 1100 Trp Leu Ser Asn Ser Ser Val Ile Pro Leu Pro Leu Pro Gly Val Ser 1110 1115 Thr Ile Pro Leu Thr Met Lys Pro Ser Ser Ser Leu Pro Thr Ile Leu 1125 1130 1135 Arg Thr Ser Ser Lys Ser Thr His Pro Ser Pro Pro Thr Thr Arg Thr 1145 1150 Ser Glu Thr Pro Val Ala Thr Thr Gln Thr Pro Thr Leu Thr Ser 1160 1155 1165 Arg Arg Thr Thr Arg Ile Thr Ser Gln Met Thr Thr Gln Ser Thr Leu 1175 1180 Thr Thr Ala Gly Thr Cys Asp Asn Gly Gly Thr Trp Glu Gln Gly 1195 1190 Gln Cys Ala Cys Leu Pro Gly Phe Ser Gly Asp Arg Cys Gln Leu Gln 1205 1210 1215 Thr Arg Cys Gln Asn Gly Gly Gln Trp Asp Gly Leu Lys Cys Gln Cys 1220 1225 1230 Pro Ser Thr Phe Tyr Gly Ser Ser Cys Glu Phe Ala Val Glu Gln Val 1240 1245 1235 Asp Leu Asp Ala Glu Asp Phe Cys Arg His Ala Gly Leu His Leu Gln 1250 1255 1260 Gly Cys Gly Asp Pro Val Pro Glu Glu Trp Gln His Arg Gly Gly Leu 1270 1275 Pro Gly Pro Ala Gly Asp Ala Leu Gln Pro Pro Ala Gly Glu Arg Val 1290

<210> 131 <211> 319 <212> PRT <213> Homo sapiens

<400> 131 Met Thr Arg Thr Tyr Glu Asn Phe Gln Tyr Leu Glu Asn Lys Val Lys 10 Val Gln Gly Phe Lys Asn Gly Pro Leu Pro Leu Gln Ser Leu Leu Gln 20 25 Arg Leu Cys Ser Gly Pro Cys His Leu Leu Leu Ser Leu Gly Leu Gly 40 Leu Leu Leu Val Ile Ile Cys Val Val Gly Phe Gln Asn Ser Lys 55 Phe Gln Arg Asp Leu Val Thr Leu Arg Thr Asp Phe Ser Asn Phe Thr 70 75 Ser Asn Thr Val Ala Glu Ile Gln Ala Leu Thr Ser Gln Gly Ser Ser 85 90 Leu Glu Glu Thr Ile Ala Ser Leu Lys Ala Glu Val Glu Gly Phe Lys 100 105 Gln Glu Arg Gln Ala Gly Val Ser Glu Leu Gln Glu His Thr Thr Gln 120 125

Lys Ala His Leu Gly His Cys Pro His Cys Pro Ser Val Cys Val Pro 135 Val His Ser Glu Met Leu Leu Arg Val Gln Gln Leu Val Gln Asp Leu 150 155 Lys Lys Leu Thr Cys Gln Val Ala Thr Leu Asn Asn Asn Gly Glu Glu 170 165 Ala Ser Thr Glu Gly Thr Cys Cys Pro Val Asn Trp Val Glu His Gln 185 Asp Ser Cys Tyr Trp Phe Ser His Ser Gly Met Ser Trp Ala Glu Ala 200 205 Glu Lys Tyr Cys Gln Leu Lys Asn Ala His Leu Val Val Ile Asn Ser 215 220 Arg Glu Glu Gln Asn Phe Val Gln Lys Tyr Leu Gly Ser Ala Tyr Thr 230 235 Trp Met Gly Leu Ser Asp Pro Glu Gly Ala Trp Lys Trp Val Asp Gly 250 Thr Asp Tyr Ala Thr Gly Phe Gln Asn Trp Lys Pro Gly Gln Pro Asp 265 Asp Trp Gln Gly His Gly Leu Gly Gly Glu Asp Cys Ala His Phe 280 285 His Pro Asp Gly Arg Trp Asn Asp Asp Val Cys Gln Arg Pro Tyr His 295 Trp Val Cys Glu Ala Gly Leu Gly Gln Thr Ser Gln Glu Ser His 310

<210> 132 <211> 590 <212> PRT

<213> Homo sapiens

Met Lys Glu Val Thr Phe His Cys His Glu Gly Tyr Ile Leu His Gly 10 Ala Pro Lys Leu Thr Cys Gln Ser Asp Gly Asn Trp Asp Ala Glu Ile 20 25 Pro Leu Cys Lys Pro Val Asn Cys Gly Pro Pro Glu Asp Leu Ala His 40 Gly Phe Pro Asn Gly Phe Ser Phe Ile His Gly Gly His Ile Gln Tyr 55 60 Gln Cys Phe Pro Gly Tyr Lys Leu His Gly Asn Ser Ser Arg Arg Cys 70 **7**5 Leu Ser Asn Gly Ser Trp Ser Gly Ser Ser Pro Ser Cys Leu Pro Cys 85 90 Arg Cys Ser Thr Pro Val Ile Glu Tyr Gly Thr Val Asn Gly Thr Asp 100 105 110 Phe Asp Cys Gly Lys Ala Ala Arg Ile Gln Cys Phe Lys Gly Phe Lys 115 120 125 Leu Leu Gly Leu Ser Glu Ile Thr Cys Glu Ala Asp Gly Gln Trp Ser 135 140 Ser Gly Phe His His Phe Glu His Thr Ser Cys Gly Ser Leu Pro Met 150 155 Ile Pro Asn Ala Phe Ile Ser Glu Thr Ser Ser Trp Lys Glu Asn Val 165 170 Ile Thr Tyr Ser Cys Arg Ser Gly Tyr Val Ile Gln Gly Ser Ser Asp 180 185 Leu Ile Cys Thr Glu Lys Gly Val Trp Ser Gln Pro Tyr Pro Val Cys 200 205 Glu Pro Leu Ser Cys Gly Ser Pro Pro Ser Val Ala Asn Ala Val Ala

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215
                                         220
Thr Gly Glu Ala His Thr Tyr Glu Ser Glu Val Lys Leu Arg Cys Leu
                 230
                                  235
Glu Gly Tyr Thr Met Asp Thr Asp Thr Arg Ser Ile Thr Cys Gln Lys
               245
                                 250
Asp Gly Arg Trp Phe Pro Glu Arg Ile Ser Cys Ser Pro Lys Lys Cys
          260
                              265
Pro Leu Pro Glu Asn Ile Thr His Ile Leu Val His Gly Asp Asp Phe
      275 280
                                            285
Ser Val Asn Arg Gln Val Ser Val Ser Cys Ala Glu Gly Tyr Thr Phe
                     295
                                        300
Glu Gly Val Asn Ile Ser Val Cys Gln Leu Asp Gly Thr Trp Glu Pro
                                    315
Pro Phe Ser Asp Glu Ser Cys Ser Pro Val Ser Cys Gly Lys Pro Glu
              325
                                 330
Ser Pro Glu His Gly Phe Val Val Gly Ser Lys Tyr Thr Phe Glu Ser
                             345
Thr Ile Ile Tyr Gln Cys Glu Pro Gly Tyr Glu Leu Glu Gly Asn Arg
                          360
Glu Arg Val Cys Gln Glu Asn Arg Gln Trp Ser Gly Gly Val Ala Ile
                      375
Cys Lys Glu Thr Arg Cys Glu Thr Pro Leu Glu Phe Leu Asn Gly Lys
                  390 395
Ala Asp Ile Glu Asn Arg Thr Thr Gly Pro Asn Val Val Tyr Ser Cys
                               410
Asn Arg Gly Tyr Ser Leu Glu Gly Pro Ser Glu Ala His Cys Thr Glu
          420
                            425
Asn Gly Thr Trp Ser His Pro Val Pro Leu Cys Lys Pro Asn Pro Cys
                         440
Pro Val Pro Phe Val Ile Pro Glu Asn Ala Leu Leu Ser Glu Lys Glu
                     455
                                        460
Phe Tyr Val Asp Gln Asn Val Ser Ile Lys Cys Arg Glu Gly Phe Leu
                  470
                                     475
Leu Gln Gly His Gly Ile Ile Thr Cys Asn Pro Asp Glu Thr Trp Thr
              485
                                490
Gln Thr Ser Ala Lys Cys Glu Lys Ile Ser Cys Gly Pro Pro Ala His
                             505
Val Glu Asn Ala Ile Ala Arg Gly Val His Tyr Gln Tyr Gly Asp Met
                         520 525
Ile Thr Tyr Ser Cys Tyr Ser Gly Tyr Met Leu Glu Gly Phe Leu Arg
                              540
                    535
Ser Val Cys Leu Glu Asn Gly Thr Trp Thr Ser Pro Pro Ile Cys Arg
                  550
                                     555
Ala Val Cys Arg Phe Pro Cys Gln Asn Gly Gly Ile Cys Gln Arg Pro
              565
                                 570
Asn Ala Cys Ser Cys Pro Glu Gly Trp Asp Gly Ala Pro Leu
                              585
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<210> 133 <211> 1544 <212> PRT <213> Homo sapiens

Lys Gln Lys Val Glu Arg Ile Ala Ser His Asp Phe Asp Pro Thr Asp 40 Ser Ser Ser Lys Lys Thr Lys Ser Ser Ser Glu Glu Ser Arg Ser Glu Ile Tyr Gly Leu Val Gln Arg Cys Val Ile Ile Gln Lys Asp Asp Asn Gly Phe Gly Leu Thr Val Ser Gly Asp Asn Pro Val Phe Val Gln Ser 90 Val Lys Glu Asp Gly Ala Ala Met Arg Ala Gly Val Gln Thr Gly Asp 100 105 Arg Ile Ile Lys Val Asn Gly Thr Leu Val Thr His Ser Asn His Leu 120 Glu Val Val Lys Leu Ile Lys Ser Gly Ser Tyr Val Ala Leu Thr Val 135 Gln Gly Arg Pro Pro Gly Ser Pro Gln Ile Pro Leu Ala Asp Ser Glu 150 155 Val Glu Pro Ser Val Ile Gly His Met Ser Pro Ile Met Thr Ser Pro 170 His Ser Pro Gly Ala Ser Gly Asn Met Glu Arg Ile Thr Ser Pro Val 185 Leu Met Gly Glu Glu Asn Asn Val Val His Asn Gln Lys Val Glu Ile 195 200 Leu Arg Lys Met Leu Gln Lys Glu Gln Glu Arg Leu Gln Leu Gln 215 Glu Asp Tyr Asn Arg Thr Pro Ala Gln Arg Leu Leu Lys Glu Ile Gln 230 235 Glu Ala Lys Lys His Ile Pro Gln Leu Gln Glu Gln Leu Ser Lys Ala 245 250 Thr Gly Ser Ala Gln Asp Gly Ala Val Val Thr Pro Ser Arg Pro Leu 265 Gly Asp Thr Leu Thr Val Ser Glu Ala Glu Thr Asp Pro Gly Asp Val 275 280 Leu Gly Arg Thr Asp Cys Ser Ser Gly Asp Ala Ser Arg Pro Ser Ser 295 300 Asp Asn Ala Asp Ser Pro Lys Ser Gly Pro Lys Glu Arg Ile Tyr Leu 310 315 Glu Glu Asn Pro Glu Lys Ser Glu Thr Ile Gln Asp Thr Asp Thr Gln 330 Ser Leu Val Gly Ser Pro Ser Thr Arg Ile Ala Pro His Ile Ile Gly 340 345 Ala Glu Asp Asp Phe Gly Thr Glu His Glu Gln Ile Asn Gly Gln 360 Cys Ser Cys Phe Gln Ser Ile Glu Leu Leu Lys Ser Arg Pro Ala His 375 Leu Ala Val Phe Leu His His Val Val Ser Gln Phe Asp Pro Ala Thr 390 395 Leu Leu Cys Tyr Leu Tyr Ser Asp Leu Tyr Lys His Thr Asn Ser Lys 410 Glu Thr Arg Arg Ile Phe Leu Glu Phe His Gln Phe Phe Leu Asp Arg 420 425 Ser Ala His Leu Lys Val Ser Val Pro Asp Glu Met Ser Ala Asp Leu 440 Glu Lys Arg Arg Pro Glu Leu Ile Pro Glu Asp Leu His Arg His Tyr 455 460 Ile Gln Thr Met Gln Glu Arg Val His Pro Glu Val Gln Arg His Leu 470 475 Lys Asp Phe Arg Gln Lys Arg Ser Met Gly Leu Thr Leu Ala Glu Ser 485 490 495 Glu Leu Thr Lys Leu Asp Ala Glu Arg Asp Lys Asp Arg Leu Thr Leu 505 Glu Lys Glu Arg Thr Cys Ala Glu Gln Ile Val Ala Lys Ile Glu Glu

520 525 Val Leu Met Thr Ala Gln Ala Val Glu Glu Asp Lys Ser Ser Thr Met 535 540 Gln Tyr Val Ile Leu Met Tyr Met Lys His Leu Gly Val Lys Val Lys · 550 Glu Pro Arg Asn Leu Glu His Lys Arg Gly Arg Ile Gly Phe Leu Pro 565 570 Lys Ile Lys Gln Ser Met Lys Lys Asp Lys Glu Gly Glu Glu Lys Gly 585 Lys Arg Arg Gly Phe Pro Ser Ile Leu Gly Pro Pro Arg Arg Pro Ser 600 Arg His Asp Asn Ser Ala Ile Gly Arg Ala Met Glu Leu Gln Lys Ala 615 620 Arg His Pro Lys His Leu Ser Thr Pro Ser Ser Val Ser Pro Glu Pro 635 630 Gln Asp Ser Ala Lys Leu Arg Gln Ser Gly Leu Ala Asn Glu Gly Thr 645 650 Asp Ala Gly Tyr Leu Pro Ala Asn Ser Met Ser Ser Val Ala Ser Gly 665 Ala Ser Phe Ser Gln Glu Gly Gly Lys Glu Asn Asp Thr Gly Ser Lys 680 685 Gln Val Gly Glu Thr Ser Ala Pro Gly Asp Thr Leu Asp Gly Thr Pro 695 700 Arg Thr Leu Asn Thr Val Phe Val Phe Pro Pro Pro Pro Leu Asp Gln 710 715 Val Gln Glu Glu Cys Glu Val Glu Arg Val Thr Glu His Gly Thr 725 730 Pro Lys Pro Phe Arg Lys Phe Asp Ser Val Ala Phe Gly Glu Ser Gln 740 745 Ser Glu Asp Glu Gln Phe Glu Asn Asp Leu Glu Thr Asp Pro Pro Asn 760 Trp Gln Gln Leu Val Ser Arg Glu Val Leu Leu Gly Leu Lys Pro Cys 775 780 Glu Ile Lys Arg Gln Glu Val Ile Asn Glu Leu Phe Tyr Thr Glu Arg 790 795 Ala His Val Arg Thr Leu Lys Val Leu Asp Gln Val Phe Tyr Gln Arg 805 810 Val Ser Arg Glu Gly Ile Leu Ser Pro Ser Glu Leu Trp Lys Ile Phe 825 Ser Asn Leu Glu Asp Ile Leu Gln Leu His Ile Gly Leu Asn Glu Gln 840 Met Lys Ala Val Arg Lys Arg Asn Glu Thr Ser Val Ile Asp Gln Ile 855 Gly Glu Asp Leu Leu Thr Trp Phe Ser Gly Pro Gly Glu Glu Lys Leu 870 875 Lys His Ala Ala Ala Thr Phe Cys Ser Asn Gln Pro Phe Ala Leu Glu 890 Met Ile Lys Ser Arg Gln Lys Lys Asp Ser Arg Phe Gln Thr Phe Val 900 905 Gln Asp Ala Glu Ser Asn Pro Leu Cys Arg Arg Leu Gln Leu Lys Asp 920 925 Ile Ile Pro Thr Gln Met Gln Arg Leu Thr Lys Tyr Pro Leu Leu Leu 935 940 Asp Asn Ile Ala Lys Tyr Thr Glu Trp Pro Thr Glu Arg Glu Lys Val 950 955 Lys Lys Ala Ala Asp His Cys Arg Gln Ile Leu Asn Tyr Val Asn Gln 965 970 Ala Val Lys Glu Ala Glu Asn Lys Gln Arg Leu Glu Asp Tyr Gln Arg 985 Arg Leu Asp Thr Ser Ser Leu Lys Leu Ser Glu Tyr Pro Asn Val Glu 1000

Glu Leu Arg Asn Leu Asp Leu Thr Lys Arg Lys Met Ile His Glu Gly 1015 1020 Pro Leu Val Trp Lys Val Asn Arg Asp Lys Thr Ile Asp Leu Tyr Thr 1030 1035 Leu Leu Glu Asp Ile Leu Val Leu Gln Lys Gln Asp Asp Arg 1045 1050 1055 Leu Val Leu Arg Cys His Ser Lys Ile Leu Ala Ser Thr Ala Asp Ser 1060 1065 1070 Lys His Thr Phe Ser Pro Val Ile Lys Leu Ser Thr Val Leu Val Arg 1075 1080 1085 Gln Gly Ala Thr Asp Asn Lys Ala Leu Phe Val Ile Ser Met Ser Asp 1095 1100 Asn Gly Ala Gln Ile Tyr Glu Leu Val Ala Gln Thr Val Ser Glu Lys 1110 1115 Thr Val Trp Gln Asp Leu Ile Cys Arg Met Ala Ala Ser Val Lys Glu 1125 1130 1135 Gln Ser Thr Lys Pro Ile Pro Leu Pro Gln Ser Thr Pro Gly Glu Gly 1140 1145 1150 Asp Asn Asp Glu Glu Asp Pro Ser Lys Leu Lys Glu Glu Gln His Gly 1155 1160 1165 Ile Ser Val Thr Gly Leu Gln Ser Pro Asp Arg Asp Leu Gly Leu Glu 1175 1180 Ser Thr Leu Ile Ser Ser Lys Pro Gln Ser His Ser Leu Ser Thr Ser 1190 1195 Gly Lys Ser Glu Val Arg Asp Leu Phe Val Ala Glu Arg Gln Phe Ala 1205 1210 Lys Glu Gln His Thr Asp Gly Thr Leu Lys Glu Val Gly Glu Asp Tyr 1220 1225 Gln Ile Ala Ile Pro Asp Ser His Leu Pro Val Ser Glu Glu Arg Trp 1235 1240 1245 Ala Leu Asp Ala Leu Arg Asn Leu Gly Leu Leu Lys Gln Leu Leu Val 1255 1260 Gln Gln Leu Gly Leu Thr Glu Lys Ser Val Gln Glu Asp Trp Gln His 1270 1275 Phe Pro Arg Tyr Arg Thr Ala Ser Gln Gly Pro Gln Thr Asp Ser Val 1285 1290 1295 Ile Gln Asn Ser Glu Asn Ile Lys Ala Tyr His Ser Gly Glu Gly His 1300 1305 1310 Met Pro Phe Arg Thr Gly Thr Gly Asp Ile Ala Thr Cys Tyr Ser Pro 1315 1320 1325 Arg Thr Ser Thr Glu Ser Phe Ala Pro Arg Asp Ser Val Gly Leu Ala 1335 1340 Pro Gln Asp Ser Gln Ala Ser Asn Ile Leu Val Met Asp His Met Ile 1350 1355 Met Thr Pro Glu Met Pro Thr Met Glu Pro Glu Gly Gly Leu Asp Asp 1370 Ser Gly Glu His Phe Phe Asp Ala Arg Glu Ala His Ser Asp Glu Asn 1380 1385 1390 Pro Ser Glu Gly Asp Gly Ala Val Asn Lys Glu Glu Lys Asp Val Asn 1400 1405 Leu Arg Ile Ser Gly Asn Tyr Leu Ile Leu Asp Gly Tyr Asp Pro Val 1415 1420 Gln Glu Ser Ser Thr Asp Glu Glu Val Ala Ser Ser Leu Thr Leu Gln 1430 1435 Pro Met Thr Gly Ile Pro Ala Val Glu Ser Thr His Gln Gln His 1445 1450 1455 Ser Pro Gln Asn Thr His Ser Asp Gly Ala Ile Ser Pro Phe Thr Pro 1460 1465 1470 Glu Phe Leu Val Gln Gln Arg Trp Gly Ala Met Glu Tyr Ser Cys Phe 1480 Glu Ile Gln Ser Pro Ser Ser Cys Ala Asp Ser Gln Ser Gln Ile Met

1490

Glu Tyr Ile His Lys Ile Glu Ala Asp Leu Glu His Leu Lys Lys Val
1505

1510

1515

1520

Glu Glu Ser Tyr Thr Ile Leu Cys Gln Arg Leu Ala Gly Ser Ala Leu
1525

Thr Asp Lys His Ser Asp Lys Ser
1540

<210> 134 <211> 486 <212> PRT <213> Homo sapiens

340

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345

Met Ala Tyr Val Asp Leu Ala Glu Thr Tyr Ala Glu Ile Gly His His 360 Arg Lys Ala Glu Glu His Phe Gln Lys Gly Leu Arg Met Lys Ile Phe 375 Glu Asp Gln Leu Lys Gln Glu Ile His Tyr His Tyr Gly Arg Phe Gln 390 395 Glu His His Gly Lys Ser Gln Asp Lys Ala Ile Thr His Tyr Leu Lys 405 410 Gly Leu Lys Ile Glu Lys Met Ser His Ser Arg Glu Lys Leu Leu Asn 425 Ala Leu Glu Lys Leu Ala Lys Arg Cys Ile His Gln Asn Val Arg Val 440 Val Glu Ser Val Ser Leu Leu Gly Leu Ile His Lys Leu Lys Gly Glu 455 Val Ser Asp Ala Leu Leu Cys Tyr Glu Arg Ala Leu Arg Leu Ala Ala 470 475 Asp Leu Asn Pro Ile Phe

<210> 135 <211> 403 <212> PRT <213> Homo sapiens

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265 Arg Leu Arg Lys Leu Glu Gly Arg Val Ala Ser Asp Glu Asp Leu Lys 280 Leu Ser Asp Met Leu Arg Tyr Tyr Met Arg Asp Ser Gln Ala Ala Lys 295 300 Asp Leu Leu Tyr Arg Arg Leu Arg Ala Leu Ala Asp Tyr Glu Asn Ala 310 315 Asn Lys Ala Leu Asp Lys Ala Arg Thr Arg Asn Arg Glu Val Arg Pro 325 330 Ala Glu Ser His Gln Gln Leu Cys Cys Gln Arg Phe Glu Arg Leu Ser 345 Asp Ser Ala Lys Gln Glu Leu Met Asp Phe Lys Ser Arg Arg Val Ser 360 Ser Phe Arg Lys Asn Leu Ile Glu Leu Ala Glu Leu Glu Leu Lys His 375 380 Ala Lys Ala Ser Thr Leu Ile Leu Arg Asn Thr Leu Val Ala Leu Lys 390 395 Gly Glu Pro

<210> 136 <211> 273 <212> PRT <213> Homo sapiens

<400> 136 Met Thr Leu Ser Pro Leu Leu Leu Phe Leu Pro Pro Leu Leu Leu 10 Leu Asp Val Pro Thr Ala Ala Val Gln Ala Ser Pro Leu Gln Ala Leu 20 25 Asp Phe Phe Gly Asn Gly Pro Pro Val Asn Tyr Lys Thr Gly Asn Leu Tyr Leu Arg Gly Pro Leu Lys Lys Ser Asn Ala Pro Leu Val Asn Val 55 Thr Leu Tyr Tyr Glu Ala Leu Cys Gly Gly Cys Arg Ala Phe Leu Ile 75 Arg Glu Leu Phe Pro Thr Trp Leu Leu Val Met Glu Ile Leu Asn Val Thr Leu Val Pro Tyr Gly Asn Ala Gln Glu Gln Asn Val Ser Gly Arg 105 Trp Glu Phe Lys Cys Gln His Gly Glu Glu Glu Cys Lys Phe Asn Lys 120 Val Glu Ala Cys Val Leu Asp Glu Leu Asp Met Glu Leu Ala Phe Leu 135 Thr Ile Val Cys Met Glu Glu Phe Glu Asp Met Glu Arg Ser Leu Pro 150 155 Leu Cys Leu Gln Leu Tyr Ala Pro Gly Leu Ser Pro Asp Thr Ile Met 170 Glu Cys Ala Met Gly Asp Arg Gly Met Gln Leu Met His Ala Asn Ala 185 Gln Arg Thr Asp Ala Leu Gln Pro Pro His Glu Tyr Val Pro Trp Val 200 205 Thr Val Asn Gly Lys Pro Leu Gly Arg Ser Asp Pro Ala Pro Tyr Pro 215 220 Cys Leu Pro Val Val Pro Gly Gln Glu Ala Gly Cys Leu Pro Phe Leu 230 235 Asn Gln Leu Pro Gln Glu Cys Leu Leu Gln Val Met Ala Gly Glu Leu

250

Arg Arg Ala His Gly Arg Arg Val Gly Thr Arg Leu Pro Ala Phe Phe 260 265 270 Phe

<210> 137 <211> 806 <212> PRT <213> Homo sapiens

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375 380 Gly Asn Tyr Thr Gln Ala Val Glu Cys Ala Lys Thr Tyr Leu Leu Phe 390 395 Phe Pro Asn Asp Glu Val Met Asn Gln Asn Leu Ala Tyr Tyr Ala Ala 405 410 Met Leu Gly Glu Glu His Thr Arg Ser Ile Gly Pro Arg Glu Ser Ala 425 420 Lys Glu Tyr Arg Gln Arg Ser Leu Leu Glu Lys Glu Leu Leu Phe Phe 440 Ala Tyr Asp Val Phe Gly Ile Pro Phe Val Asp Pro Asp Ser Trp Thr 455 Pro Glu Glu Val Ile Pro Lys Arg Leu Gln Glu Lys Gln Lys Ser Glu 470 475 Arg Glu Thr Ala Val Arg Ile Ser Gln Glu Ile Gly Asn Leu Met Lys 490 495 485 Glu Ile Glu Thr Leu Val Glu Glu Lys Thr Lys Glu Ser Leu Asp Val ₫ 505 Ser Arg Leu Thr Arg Glu Gly Gly Pro Leu Leu Tyr Glu Gly Ile Ser 515 | 520 525 Leu Thr Met Asn Ser Lys Leu Leu Asn Gly Ser Gln Arg Val Val Met 540 535 Asp Gly Val Ile Ser Asp His Glu Cys Gln Glu Leu Gln Arg Leu Thr 550 555 Asn Val Ala Ala Thr Ser Gly Asp Gly Tyr Arg Gly Gln Thr Ser Pro 575 565 570 His Thr Pro Asn Glu Lys Phe Tyr Gly Val Thr Val Phe Lys Ala Leu 580 585 Lys Leu Gly Gln Glu Gly Lys Val Pro Leu Gln Ser Ala His Leu Tyr 600 Tyr Asn Val Thr Glu Lys Val Arg Arg Ile Met Glu Ser Tyr Phe Arg 615 620 Leu Asp Thr Pro Leu Tyr Phe Ser Tyr Ser His Leu Val Cys Arg Thr 635 630 Ala Ile Glu Glu Val Gln Ala Glu Arg Lys Asp Asp Ser His Pro Val 650 His Val Asp Asn Cys Ile Leu Asn Ala Glu Thr Leu Val Cys Val Lys 665 670 Glu Pro Pro Ala Tyr Thr Phe Arg Asp Tyr Ser Ala Ile Leu Tyr Leu 680 Asn Gly Asp Phe Asp Gly Gly Asn Phe Tyr Phe Thr Glu Leu Asp Ala 695 700 Lys Thr Val Thr Ala Glu Val Gln Pro Gln Cys Gly Arg Ala Val Gly 710 715 Phe Ser Ser Gly Thr Glu Asn Pro His Gly Val Lys Ala Val Thr Arg 730 725 Gly Gln Arg Cys Ala Ile Ala Leu Trp Phe Thr Leu Asp Pro Arg His 745 Ser Glu Arg Asp Arg Val Gln Ala Asp Asp Leu Val Lys Met Leu Phe 760 Ser Pro Glu Glu Met Asp Leu Ser Gln Glu Gln Pro Leu Asp Ala Gln 775 780 Gln Gly Pro Pro Glu Pro Ala Gln Glu Ser Leu Ser Gly Ser Glu Ser 795 Lys Pro Lys Asp Glu Leu 805

<210> 138 <211> 244 <212> PRT

<213> Homo sapiens

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<210> 139 <211> 538 <212> PRT

<213> Homo sapiens

<400> 139 Met Ala Leu Tyr Asp Glu Asp Leu Leu Lys Asn Pro Phe Tyr Leu Ala 10 Leu Gln Lys Cys Arg Pro Asp Leu Cys Ser Lys Val Ala Gln Ile His 25 Gly Ile Val Leu Val Pro Cys Lys Gly Ser Leu Ser Ser Ser Ile Gln 40 Ser Thr Cys Gln Phe Glu Ser Tyr Ile Leu Ile Pro Val Glu Glu His 55 60 Phe Gln Thr Leu Asn Gly Lys Asp Val Phe Ile Gln Gly Asn Arg Ile Lys Leu Gly Ala Gly Phe Ala Cys Leu Leu Ser Val Pro Ile Leu Phe 90 Glu Glu Thr Phe Tyr Asn Glu Lys Glu Glu Ser Phe Ser Ile Leu Cys 105 Ile Ala His Pro Leu Glu Lys Arg Glu Ser Ser Glu Glu Pro Leu Ala

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115
                          120
Pro Ser Asp Pro Phe Ser Leu Lys Thr Ile Glu Asp Val Arg Glu Phe
            135
                                        140
Leu Gly Arg His Ser Glu Arg Phe Asp Arg Asn Ile Ala Ser Phe His
                  150
                                     155
Arg Thr Phe Arg Glu Cys Glu Arg Lys Ser Leu Arg His His Ile Asp
         · 165
                                 170
Ser Ala Asn Ala Leu Tyr Thr Lys Cys Leu Gln Gln Leu Leu Arg Asp
          180
                              185
Ser His Leu Lys Met Leu Ala Lys Gln Glu Ala Gln Met Asn Leu Met
                          200
Lys Gln Ala Val Glu Ile Tyr Val His His Glu Ile Tyr Asn Leu Ile
                      215
                                        220
Phe Lys Tyr Val Gly Thr Met Glu Ala Ser Glu Asp Ala Ala Phe Asn
                  230
                                     235
Lys Ile Thr Arg Ser Leu Gln Asp Leu Gln Gln Lys Asp Ile Gly Val
              245
                      250
Lys Pro Glu Phe Ser Phe Asn Ile Pro Arg Ala Lys Arg Glu Leu Ala
                             265
Gln Leu Asn Lys Cys Thr Ser Pro Gln Gln Lys Leu Val Cys Leu Arg
                          280
Lys Val Val Gln Leu Ile Thr Gln Ser Pro Ser Gln Arg Val Asn Leu
                      295
                              300
Glu Thr Met Cys Ala Asp Asp Leu Leu Ser Val Leu Leu Tyr Leu Leu
                  310
                                     315
Val Lys Thr Glu Ile Pro Asn Trp Met Ala Asn Leu Ser Tyr Ile Lys
              325
                                 330
Asn Phe Arg Phe Ser Ser Leu Ala Lys Asp Glu Leu Gly Tyr Cys Leu
          340
                             345
Thr Ser Phe Glu Ala Ala Ile Glu Tyr Ile Arg Gln Gly Ser Leu Ser
                          360
                                 · 365
Ala Lys Pro Pro Glu Ser Glu Gly Phe Gly Asp Arg Leu Phe Leu Lys
                      375
                                         380
Gln Arg Met Ser Leu Leu Ser Gln Met Thr Ser Ser Pro Thr Asp Cys
                  390
                                     395
Leu Phe Lys His Ile Ala Ser Gly Asn Gln Lys Glu Val Glu Arg Leu
                                410
Leu Ser Gln Glu Asp His Asp Lys Asp Thr Val Gln Lys Met Cys His
          420
                             425
Pro Leu Cys Phe Cys Asp Asp Cys Glu Lys Leu Val Ser Gly Arg Leu
    435
                          440
Asn Asp Pro Ser Val Val Thr Pro Phe Ser Arg Asp Asp Arg Gly His
                      455
                                         460
Thr Pro Leu His Val Ala Ala Val Cys Gly Gln Ala Ser Leu Ile Asp
                  470
                                     475
Leu Leu Val Ser Lys Gly Ala Met Val Asn Ala Thr Asp Tyr His Gly
                                 490
Ala Thr Pro Leu His Leu Ala Cys Gln Lys Gly Tyr Gln Ser Val Thr
                             505
Leu Leu Leu His Tyr Lys Ala Ser Ala Glu Val Gln Asp Asn Asn
                         520
Gly Asn Thr Pro His Val Leu Arg Pro Leu
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<210> 140

<211> 232

<212> PRT

<213> Homo sapiens

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<210> 141 <211> 105 <212> PRT <213> Homo sapiens

<210> 142 <211> 333

<212> PRT <213> Homo sapiens

<400> 142 Met Asn Leu Ser Leu Val Leu Ala Ala Phe Cys Leu Gly Ile Ala Ser Ala Val Pro Lys Phe Asp Gln Asn Leu Asp Thr Lys Trp Tyr Gln Trp 20 25 Lys Ala Thr His Arg Arg Leu Tyr Gly Ala Asn Glu Glu Gly Trp Arg 35 40 Arg Ala Val Trp Glu Lys Asn Met Lys Met Ile Glu Leu His Asn Gly 55 60 Glu Tyr Ser Gln Gly Lys His Ser Phe Thr Met Ala Met Asn Ala Phe 70 Gly Asp Met Thr Asn Glu Glu Phe Arg Gln Val Met Asn Gly Phe Gln . 90 85 Tyr Gln Lys His Arg Lys Gly Lys Gln Phe Gln Glu Arg Leu Leu 105 Glu Ile Pro Thr Ser Val Asp Trp Arg Glu Lys Gly Tyr Met Thr Pro 120 125 Val Lys Asp Gln Gly Gln Cys Gly Ser Cys Trp Ala Phe Ser Ala Thr 135 140 Gly Ala Leu Glu Gly Gln Met Phe Trp Lys Thr Gly Lys Leu Ile Ser 150 155 Leu Asn Glu Gln Asn Leu Val Asp Cys Ser Gly Pro Gln Gly Asn Glu 170 Gly Cys Asn Gly Asp Phe Met Asp Asn Pro Phe Arg Tyr Val Gln Glu 180 185 Asn Gly Gly Leu Asp Ser Glu Glu Ser Tyr Pro Tyr Glu Ala Thr Glu 200 Glu Ser Cys Lys Tyr Asn Pro Lys Tyr Ser Val Ala Asn Asp Thr Gly 215 220 Phe Val Asp Ile Pro Lys Gln Glu Lys Ala Leu Met Lys Ala Val Ala 230 235 Thr Val Gly Pro Ile Ser Val Ala Ile Asp Ala Gly His Glu Ser Phe 245 250 Leu Phe Tyr Lys Glu Gly Ile Tyr Phe Glu Pro Asp Cys Ser Ser Glu 265 Asp Met Asp His Gly Val Leu Val Val Gly Tyr Gly Phe Glu Ser Thr 275 280 Glu Ser Asp Asn Asn Lys Tyr Trp Leu Val Lys Asn Ser Trp Gly Glu . 300 295 Glu Trp Gly Met Gly Gly Tyr Val Lys Met Ala Lys Asp Arg Arg Asn His Cys Gly Ile Ala Ser Ala Ala Ser Tyr Pro Thr Val 325 330

<210> 143 <211> 208 <212> PRT <213> Homo sapiens

<400> 143
Met Leu Gly Cys Gln Gly Arg Met Tyr Thr Leu Leu Ser Gly Leu Tyr
1 5 10 15
Lys Tyr Met Phe Gln Lys Asp Glu Tyr Cys Ile Leu Ile Leu Gly Leu
20 25 30

Asp Asn Ala Gly Lys Thr Thr Phe Leu Glu Gln Ser Lys Thr Arg Phe Asn Lys Asn Tyr Lys Gly Met Ser Leu Ser Lys Ile Thr Thr Val 55 Gly Leu Asn Ile Gly Thr Val Asp Val Gly Lys Ala Arg Leu Met Phe 70 75 Trp Asp Leu Gly Gly Gln Glu Glu Leu Gln Ser Leu Trp Asp Lys Tyr 90 Tyr Ala Glu Cys His Gly Val Ile Tyr Val Ile Asp Ser Thr Asp Glu 100 105 Glu Arg Leu Ala Glu Ser Lys Gln Ala Phe Glu Lys Val Val Thr Ser 120 125 Glu Ala Leu Cys Gly Val Pro Val Leu Val Leu Ala Asn Lys Gln Asp 135 140 Val Glu Thr Cys Leu Ser Ile Pro Asp Ile Lys Thr Ala Phe Ser Asp 150 155 Cys Thr Ser Lys Ile Gly Arg Arg Asp Cys Leu Thr Gln Ala Cys Ser 165 170 Ala Leu Thr Gly Lys Gly Val Arg Glu Gly Ile Glu Trp Met Val Lys 185 Cys Val Val Arg Asn Val His Arg Pro Pro Arg Gln Arg Asp Ile Thr

<210> 144 <211> 229 <212> PRT <213> Homo sapiens

<400> 144 Met Leu Ser Val Asp Ile Thr Ser Arg Tyr Arg Ala Pro Ser Thr Tyr 10 Leu Leu Asn Ser Leu Lys Glu Gly Leu Glu Gly Leu His Gly Glu Ser 25 Cys Ser Ser Phe Leu Leu Gly Pro Ser Val Ala Met Asn Met Gln Thr 40 Ala Gly Leu Glu Met Asp Ile Cys Asp Gly His Phe Arg Gln Asn Gly 55 Gly Cys Gly Tyr Val Leu Lys Pro Asp Phe Leu Arg Asp Ile Gln Ser 70 75 Ser Phe His Pro Glu Lys Pro Ile Ser Pro Phe Lys Ala Gln Thr Leu 90 Leu Ile Gln Val Ile Ser Gly Gln Gln Leu Pro Lys Val Asp Lys Thr 105 Lys Glu Gly Ser Ile Val Asp Pro Leu Val Lys Val Gln Ile Phe Gly 120 125 Val Arg Leu Asp Thr Ala Arg Gln Glu Thr Asn Tyr Val Glu Asn Asn 135 140 Gly Phe Asn Pro Tyr Trp Gly Gln Thr Leu Cys Phe Arg Val Leu Val 150 Pro Glu Leu Ala Met Leu Arg Phe Val Val Met Asp Tyr Asp Trp Lys 165 170 175 Ser Arg Asn Asp Phe Ile Gly Gln Tyr Thr Leu Pro Trp Thr Cys Met 190 185 ' Gln Gln Gly Tyr Arg His Ile His Leu Leu Ser Lys Asp Gly Ile Ser 200 Leu Arg Pro Ala Ser Ile Phe Val Tyr Ile Cys Ile Gln Glu Gly Leu

210 215 220 Glu Gly Asp Glu Ser 225

<210> 145 <211> 223 <212> PRT <213> Homo sapiens

<400> 145 Met Arg Gly Pro Gly Gln Ala Asp Cys Ala Val Ala Ile Gly Arg Pro 10 Leu Gly Glu Val Val Thr Leu Arg Val Leu Glu Ser Ser Leu Asn Cys 20 25 Ser Ala Gly Asp Met Leu Leu Leu Trp Gly Arg Leu Thr Trp Arg Lys 35 40 Met Cys Arg Lys Leu Leu Asp Met Thr Phe Ser Ser Lys Thr Asn Thr 55 60 Leu Val Val Arg Gln Arg Cys Gly Arg Pro Gly Gly Val Leu Leu 70 75 Arg Tyr Gly Ser Gln Leu Ala Pro Glu Thr Phe Tyr Arg Glu Cys Asp 85 90 Met Gln Leu Phe Gly Pro Trp Gly Glu Ile Val Ser Pro Ser Leu Ser 105 Pro Ala Thr Ser Asn Ala Gly Gly Cys Arg Leu Phe Ile Asn Val Ala 120 125 Pro His Ala Arg Ile Ala Ile His Ala Leu Ala Thr Asn Met Gly Ala 135 140 Gly Thr Glu Gly Ala Asn Ala Ser Tyr Ile Leu Ile Arg Asp Thr His 150 155 Ser Leu Arg Thr Thr Ala Phe His Gly Gln Gln Val Leu Tyr Trp Glu 165 170 Ser Glu Ser Ser Gln Ala Glu Met Glu Phe Ser Glu Gly Phe Leu Lys 185 Ala Gln Ala Ser Leu Arg Gly Gln Tyr Trp Thr Leu Gln Ser Trp Val 200 Pro Glu Met Gln Asp Pro Gln Ser Trp Lys Gly Lys Glu Gly Thr

<210> 146 <211> 73 <212> PRT <213> Homo sapiens

<210> 147 <211> 202 <212> PRT <213> Homo sapiens

<400> 147 Met Ala Glu Tyr Leu Ala Ser Ile Phe Gly Thr Glu Lys Asp Lys Val 10 Asn Cys Ser Phe Tyr Phe Lys Ile Gly Val Cys Arg His Gly Asp Arg 20 Cys Ser Arg Leu His Asn Lys Pro Thr Phe Ser Gln Glu Val Phe Thr 40 Glu Leu Gln Glu Lys Tyr Gly Glu Ile Glu Glu Met Asn Val Cys Asp 55 Asn Leu Gly Asp His Leu Val Gly Asn Val Tyr Val Lys Phe Arg Arg 70 Glu Glu Asp Gly Glu Arg Ala Val Ala Glu Leu Ser Asn Arg Trp Phe 85 90 Asn Gly Gln Ala Val His Gly Asn Val Pro Glu Val Ala Ser Ala Thr 105 Ser Cys Ile Cys Gly Pro Phe Pro Arg Thr Ser Arg Gly Ser Ser Met 120 125 Gly Gly Asp Pro Gly Ala Gly His Pro Arg Gly Ser Ile Leu Ala Thr 135 Ile Pro Glu Arg Gly Thr Ile Gly Val Pro Leu Ile Thr Gly Met Ala 150 155 Ala Ser Glu Ala Leu Ala Pro Leu Pro Phe Thr Pro Asn Arg Asp Arg 165 170 175 Cys Ser Trp Gln Asp Leu Ser Ser Lys Pro Pro Ser Leu Ser Cys Pro 180 185 Ile Leu Pro Arg Leu Pro Gly Ser Ile Met

<210> 148 <211> 241 <212> PRT <213> Homo sapiens

<400> 148 Met Ala Glu Tyr Leu Ala Ser Ile Phe Gly Thr Glu Lys Asp Lys Val 5 10 Asn Cys Ser Phe Tyr Phe Lys Ile Gly Ala Cys Arg His Gly Asp Arg 20 25 Cys Ser Arg Leu His Asn Lys Pro Thr Phe Ser Gln Thr Ile Val Leu 40 Leu Asn Leu Tyr Arg Asn Pro Gln Asn Thr Ala Gln Thr Ala Asp Gly 60 Ser His Cys His Val Ser Asp Val Glu Val Gln Glu His Tyr Asp Ser 70 Phe Phe Glu Glu Val Phe Thr Glu Leu Gln Glu Lys Tyr Gly Glu Ile 85 90 Glu Glu Met Asn Val Cys Asp Asn Leu Gly Asp His Leu Val Gly Asn 105 Val Tyr Val Lys Phe Arg Arg Glu Glu Asp Gly Glu Arg Ala Val Ala

120 115 125 Glu Leu Ser Asn Arg Trp Phe Asn Gly Gln Ala Val His Gly Asn Val 135 140 Pro Glu Val Ala Ser Ala Thr Ser Cys Ile Cys Gly Pro Phe Pro Arg 150 155 Thr Ser Arg Gly Ser Ser Met Gly Gly Asp Pro Gly Ala Gly His Pro 170 Arg Gly Ser Ile Leu Ala Thr Ile Pro Glu Arg Gly Thr Ile Val Val 185 190 Pro Leu Ile Thr Gly Met Ala Ala Ser Glu Ala Leu Ala Pro Leu Pro 200 Phe Thr Pro Asn Arg Asp Arg Cys Ser Trp Gln Asp Leu Ser Ser Lys 215 220 Pro Pro Ser Leu Ser Cys Pro Ile Leu Pro Arg Leu Pro Gly Ser Ile 230 235 Met

<210> 149 <211> 794 <212> PRT <213> Homo sapiens

<400> 149 Met Leu Cys Gly Arg Trp Arg Arg Cys Arg Arg Pro Pro Glu Glu Pro 10 Pro Val Ala Ala Gln Val Ala Ala Gln Val Ala Pro Val Ala Leu 20 25 Pro Ser Pro Pro Thr Pro Ser Asp Gly Gly Thr Lys Arg Pro Gly Leu 40 Arg Ala Leu Lys Lys Met Gly Leu Thr Glu Asp Glu Asp Val Arg Ala Met Leu Arg Gly Ser Arg Leu Arg Lys Ile Arg Ser Arg Thr Trp His 70 Lys Glu Arg Leu Tyr Arg Leu Gln Glu Asp Gly Leu Ser Val Trp Phe Gln Arg Arg Ile Pro Arg Ala Pro Ser Gln His Ile Phe Phe Val Gln 105 His Ile Glu Ala Val Arg Glu Gly His Gln Ser Glu Gly Leu Arg Arg 120 125 Phe Gly Gly Ala Phe Ala Pro Ala Arg Cys Leu Thr Ile Ala Phe Lys 135 140 Gly Arg Arg Lys Asn Leu Asp Leu Ala Ala Pro Thr Ala Glu Glu Ala 150 Gln Arg Trp Val Arg Gly Leu Thr Lys Leu Arg Ala Arg Leu Asp Ala 165 170 Met Ser Gln Arg Glu Arg Leu Asp His Trp Ile His Ser Tyr Leu His 185 Arg Ala Asp Ser Asn Gln Asp Ser Lys Met Ser Phe Lys Glu Ile Lys 200 Ser Leu Leu Arg Met Val Asn Val Asp Met Asn Asp Met Tyr Ala Tyr 215 220 Leu Leu Phe Lys Glu Cys Asp His Ser Asn Asn Asp Arg Leu Glu Gly 230 235 Ala Glu Ile Glu Glu Phe Leu Arg Arg Leu Leu Lys Arg Pro Glu Leu 250 Glu Glu Ile Phe His Gln Tyr Ser Gly Glu Asp Arg Val Leu Ser Ala 265 260

Pro Glu Leu Leu Glu Phe Leu Glu Asp Gln Gly Glu Gly Ala Thr 280 Leu Ala Arg Ala Gln Gln Leu Ile Gln Thr Tyr Glu Leu Asn Glu Thr 295 Ala Lys Gln His Glu Leu Met Thr Leu Asp Gly Phe Met Met Tyr Leu 310 315 Leu Ser Pro Glu Gly Ala Ala Leu Asp Asn Thr His Thr Cys Val Phe 325 330 Gln Asp Met Asn Gln Pro Leu Ala His Tyr Phe Ile Ser Ser His 340 345 Asn Thr Tyr Leu Thr Asp Ser Gln Ile Gly Gly Pro Ser Ser Thr Glu 360 Ala Tyr Val Arg Tyr Cys Ser Arg Gly Ala Phe Ala Gln Gly Cys Arg 375 Cys Val Glu Leu Asp Cys Trp Glu Gly Pro Gly Glu Pro Val Ile 390 395 Tyr His Gly His Thr Leu Thr Ser Lys Ile Leu Phe Arg Asp Val Val · 405 410 Gln Ala Val Arg Asp His Ala Phe Thr Leu Ser Pro Tyr Pro Val Ile 425 Leu Ser Leu Glu Asn His Cys Gly Leu Glu Gln Gln Ala Ala Met Ala 440 445 Arg His Leu Cys Thr Ile Leu Gly Asp Met Leu Val Thr Gln Ala Leu 455 460 Asp Ser Pro Asn Pro Glu Glu Leu Pro Ser Pro Glu Gln Leu Lys Gly 470 475 Arg Val Leu Val Lys Gly Lys Lys Leu Pro Ala Ala Arg Ser Glu Asp 485 490 Gly Arg Ala Leu Ser Asp Arg Glu Glu Glu Glu Asp Asp Glu Glu 505 Glu Glu Glu Glu Val Glu Ala Ala Ala Gln Arg Arg Leu Ala Lys Gln 520 Ile Ser Pro Glu Leu Ser Ala Leu Ala Val Tyr Cys His Ala Thr Arg 535 Leu Arg Thr Leu His Pro Ala Pro Asn Ala Pro Gln Pro Cys Gln Val 550 555 Ser Ser Leu Ser Glu Arg Lys Ala Lys Lys Leu Ile Arg Glu Ala Gly 565 570 Asn Ser Phe Val Arg His Asn Ala Arg Gln Leu Thr Arg Val Tyr Pro 585 Leu Gly Leu Arg Met Asn Ser Ala Asn Tyr Ser Pro Gln Glu Met Trp 600 Asn Ser Gly Cys Gln Leu Val Ala Leu Asn Phe Gln Thr Pro Gly Tyr 615 620 Glu Met Asp Leu Asn Ala Gly Arg Phe Leu Val Asn Gly Gln Cys Gly 630 635 Tyr Val Leu Lys Pro Ala Cys Leu Arg Gln Pro Asp Ser Thr Phe Asp 645 650 Pro Glu Tyr Pro Gly Pro Pro Arg Thr Thr Leu Ser Ile Gln Val Leu 665 Thr Ala Gln Gln Leu Pro Lys Leu Asn Ala Glu Lys Pro His Ser Ile 680 Val Asp Pro Leu Val Arg Ile Glu Ile His Gly Val Pro Ala Asp Cys 695 700 Ala Arg Gln Glu Thr Asp Tyr Val Leu Asn Asn Gly Phe Asn Pro Arg 710 715 Trp Gly Gln Thr Leu Gln Phe Gln Leu Arg Ala Pro Glu Leu Ala Leu 725 730 Val Arg Phe Val Val Glu Asp Tyr Asp Ala Thr Ser Pro Asn Asp Phe 745 Val Gly Gln Phe Thr Leu Pro Leu Ser Ser Leu Lys Gln Gly Tyr Arg

760 His Ile His Leu Leu Ser Lys Asp Gly Ala Ser Leu Ser Pro Ala Thr 775 780 Leu Phe Ile Gln Ile Arg Ile Gln Arg Ser 790

<210> 150 <211> 115 <212> PRT <213> Homo sapiens

<400> 150 Met Ala Ala Val Pro Met Val Leu Ser Ala Met Gly Phe Thr Ala Ala 5 10 Gly Ile Ala Ser Ser Ser Ile Ala Ala Lys Met Met Ser Ala Ala Ala 20 25 Ile Ala Asn Gly Gly Gly Val Ser Ala Gly Ser Leu Val Ala Thr Leu 40 Gln Ser Val Gly Ala Ala Gly Leu Ser Thr Ser Ser Asn Ile Leu Leu 55 60 Ala Ser Val Gly Ser Val Leu Gly Ala Cys Leu Gly Asn Ser Pro Ser 70 75 Ser Ser Leu Pro Ala Glu Pro Glu Ala Lys Glu Asp Glu Ala Arg Glu Asn Val Pro Gln Gly Glu Pro Pro Lys Pro Pro Leu Lys Ser Glu Lys 105 · 110 His Glu Glu 115

<210> 151 <211> 294 <212> PRT <213> Homo sapiens

<400> 151 Met Ala Gln Ala Pro Ala Asp Pro Gly Arg Glu Ala Lys Arg Pro Gln 1 5 10 Gln His Ala Ala Thr Ile Pro Glu Thr Pro Gly Pro Gln Phe Ser Gln 25 Gln Arg Glu Glu Asp Ile Tyr Arg Phe Leu Lys Asp Asn Gly Pro Gln 40 45 Arg Ala Leu Val Ile Ala Gln Ala Leu Gly Met Arg Thr Ala Lys Asp 55 Val Asn Arg Asp Leu Tyr Arg Met Lys Ser Arg His Leu Leu Asp Met Asp Glu Gln Ser Lys Ala Trp Thr Ile Tyr Arg Pro Glu Asp Ser Gly 85 90 Arg Arg Ala Lys Ser Ala Ser Ile Ile Tyr Gln His Asn Pro Ile Asn 105 100 Met Ile Cys Gln Asn Gly Pro Asn Ser Trp Ile Ser Ile Ala Asn Ser 120 Glu Ala Ile Gln Ile Gly His Gly Asn Ile Ile Thr Arg Gln Thr Val 135 140 Ser Arg Glu Asp Gly Ser Ala Gly Pro Arg His Leu Pro Ser Met Ala 150

155

Pro Gly Asp Ser Ser Thr Trp Gly Thr Leu Val Asp Pro Trp Gly Pro 165 170 Gln Asp Ile His Met Glu Arg Ser Ile Leu Arg Arg Val Gln Leu Gly 185 His Ser Asn Glu Met Arg Leu His Gly Val Pro Ser Glu Gly Pro Ala 200 His Ile Pro Pro Gly Ser Pro Pro Val Ser Ala Thr Ala Ala Gly Pro 215 220 Glu Ala Ser Phe Glu Ala Arg Ile Pro Ser Pro Gly Thr His Pro Glu 230 235 Gly Glu Ala Ala Gln Arg Ile His Met Lys Ser Cys Phe Leu Glu Asp 250 Ala Thr Ile Gly Asn Ser Asn Lys Met Ser Ile Gln Pro Arg Gly Gly 265 Trp Pro Arg Arg Ser Arg Arg Val Trp Arg Gly Gly Ala Arg Gly Gly Arg Ser Cys Cys Leu His 290

<210> 152 <211> 328 <212> PRT <213> Homo sapiens

<400> 152 Met Ser Val Arg Ser Lys Leu Pro Asn Ser Pro Ala Ala Ser Ser His Pro Lys Leu Lys Ser Ser Lys Gly Ile Thr Lys Lys Pro Gln Ala Pro 20 25 Ser Asn Asn Ala Ser Ser Ser Leu Ala Ser Leu Asn Pro Val Gly Lys 40 Asn Thr Ser Ser Pro Ala Leu Pro Arg Thr Ala Pro Cys Ile Ser Glu 55 Ser Pro Arg Lys Cys Ile Ser Ser Pro Asn Thr Pro Lys Ala Lys Val 70 Ile Pro Ala Gln Asn Ser Ala Asp Leu Pro Glu Ser Thr Leu Leu Pro 85 90 Asn Lys Cys Ser Gly Lys Thr Gln Pro Lys Tyr Leu Lys His Asn His 105 Ile Ser Ser Arg Asp Asn Ala Val Ser His Leu Ala Ala His Ser Asn 120 Ser Ser Ser Lys Cys Pro Lys Leu Pro Lys Ala Asn Ile Pro Val Arg 135 140 Pro Lys Pro Ser Phe Gln Ser Ser Ala Lys Met Thr Lys Thr Ser Ser 150 155 Lys Thr Ile Ala Thr Gly Leu Gly Thr Gln Ser Gln Pro Ser Asp Gly 165 170 Ala Pro Gln Ala Lys Pro Val Pro Ala Gln Lys Leu Lys Ser Ala Leu 185 Asn Leu Asn Gln Pro Val Ser Val Ser Ser Val Ser Pro Val Lys Ala 200 Thr Gln Lys Ser Lys Asp Lys Asn Ile Val Ser Ala Thr Lys Lys Gln 215 Pro Gln Asn Lys Ser Ala Phe Gln Lys Thr Gly Pro Ser Ser Leu Lys 230 235 Ser Pro Gly Arg Thr Pro Leu Ser Ile Val Ser Leu Pro Gln Ser Ser 245 250 Thr Lys Thr Gln Thr Ala Pro Lys Ser Ala Gln Thr Val Ala Lys Ser

<210> 153 <211> 1651 <212> PRT <213> Homo sapiens

<400> 153 Met Ala Pro Thr Leu Phe Gln Lys Leu Phe Ser Lys Arg Thr Gly Leu 5 10 Gly Ala Pro Gly Arg Asp Ala Arg Asp Pro Asp Cys Gly Phe Ser Trp 25 Pro Leu Pro Glu Phe Asp Pro Ser Gln Ile Arg Leu Ile Val Tyr Gln 45 Asp Cys Glu Arg Arg Gly Arg Asn Val Leu Phe Asp Ser Ser Val Lys 55 60 Arg Arg Asn Glu Asp Ile Ser Val Ser Asp Leu Asn Thr Ile Tyr Ser 70 75 Tyr Leu His Gly Met Glu Ile Leu Ser Asn Leu Arg Glu His Gln Leu 85 90 Arg Leu Met Ser Ala Arg Ala Arg Tyr Glu Arg Tyr Ser Gly Asn Gln 100 105 Val Leu Phe Cys Ser Glu Thr Ile Ala Arg Cys Trp Tyr Ile Leu Leu 120 125 Ser Gly Ser Val Leu Val Lys Gly Ser Met Val Leu Pro Pro Cys Ser 135 Phe Gly Lys Gln Phe Gly Gly Lys Arg Gly Cys Asp Cys Leu Val Leu 150 155 Glu Pro Ser Glu Met Ile Val Val Glu Asn Ala Lys Asp Asn Glu Asp 165 170 Ser Ile Leu Gln Arg Glu Ile Pro Ala Arg Gln Ser Arg Arg Phe 185 Arg Lys Ile Asn Tyr Lys Gly Glu Arg Gln Thr Ile Thr Asp Asp Val 200 Glu Val Asn Ser Tyr Leu Ser Leu Pro Ala Asp Leu Thr Lys Met His 215 220 Leu Thr Glu Asn Pro His Pro Gln Val Thr His Val Ser Ser Ser Gln 230 235 Ser Gly Cys Ser Ile Ala Ser Asp Ser Gly Ser Ser Ser Leu Ser Asp 245 250 Ile Tyr Gln Ala Thr Glu Ser Glu Val Gly Asp Val Asp Leu Thr Arg 265 Leu Pro Glu Gly Pro Val Asp Ser Glu Asp Asp Glu Glu Glu Asp Glu 280 Glu Ile Asp Arg Thr Asp Pro Leu Gln Gly Arg Asp Leu Val Arg Glu 295 300 Cys Leu Glu Lys Glu Pro Ala Asp Lys Thr Asp Asp Ile Glu Gln 310 315 Leu Leu Glu Phe Met His Gln Leu Pro Ala Phe Ala Asn Met Thr Met 325 330

Ser Val Arg Arg Glu Leu Cys Ser Val Met Ile Phe Glu Val Val Glu 345 Gln Ala Gly Ala Ile Ile Leu Glu Asp Gly Gln Glu Leu Asp Ser Trp 355 360 Tyr Val Ile Leu Asn Gly Thr Val Glu Ile Ser His Pro Asp Gly Lys 375 380 Val Glu Asn Leu Phe Met Gly Asn Ser Phe Gly Ile Thr Pro Thr Leu 390 395 Asp Lys Gln Tyr Met His Gly Ile Val Arg Thr Lys Val Asp Asp Cys 405 410 Gln Phe Val Cys Ile Ala Gln Gln Asp Tyr Trp Arg Ile Leu Asn His 420 425 Val Glu Lys Asn Thr His Lys Val Glu Glu Glu Gly Glu Ile Val Met 440 Val His Glu His Arg Glu Leu Asp Arg Ser Gly Thr Arg Lys Gly His 455 460 Ile Val Ile Lys Ala Thr Pro Glu Arg Leu Ile Met His Leu Ile Glu 470 475 Glu His Ser Ile Val Asp Pro Thr Tyr Ile Glu Asp Phe Leu Leu Thr 485 490 Tyr Arg Thr Phe Leu Glu Ser Pro Leu Asp Val Gly Ile Lys Leu Leu 505 Glu Trp Phe Lys Ile Asp Ser Leu Arg Asp Lys Val Thr Arg Ile Val 520 Leu Leu Trp Val Asn Asn His Phe Asn Asp Phe Glu Gly Asp Pro Ala 535 Met Thr Arg Phe Leu Glu Glu Phe Glu Lys Asn Leu Glu Asp Thr Lys 550 555 Met Asn Gly His Leu Arg Leu Leu Asn Ile Ala Cys Ala Ala Lys Ala 565 570 Lys Trp Arg Gln Val Val Leu Gln Lys Ala Ser Arg Glu Ser Pro Leu 585 Gln Phe Ser Leu Asn Gly Gly Ser Glu Lys Gly Phe Gly Ile Phe Val 600 Glu Gly Val Glu Pro Gly Ser Lys Ala Ala Asp Ser Gly Leu Lys Arg 620 Gly Asp Gln Ile Met Glu Val Asn Gly Gln Asn Phe Glu Asn Ile Thr 630 635 Phe Met Lys Ala Val Glu Ile Leu Arg Asn Asn Thr His Leu Ala Leu 645 650 Thr Val Lys Thr Asn Ile Phe Val Phe Lys Glu Leu Leu Phe Arg Thr 660 665 Glu Glu Lys Ser Gly Val Pro His Ile Pro Lys Ile Ala Glu Lys 680 685 Lys Ser Asn Arg His Ser Ile Gln His Val Pro Gly Asp Ile Glu Gln 695 700 Thr Ser Gln Glu Lys Gly Ser Lys Lys Val Lys Ala Asn Thr Val Ser 710 715 Gly Gly Arg Asn Lys Ile Arg Lys Ile Leu Asp Lys Thr Arg Phe Ser 725 730 Ile Leu Pro Pro Lys Leu Phe Ser Asp Gly Gly Leu Ser Gln Ser Gln 745 Asp Asp Ser Ile Val Gly Thr Arg His Cys Arg His Ser Leu Ala Ile 760 765 Met Pro Ile Pro Gly Thr Leu Ser Ser Ser Pro Asp Leu Leu Gln 775 • 780 Pro Thr Thr Ser Met Leu Asp Phe Ser Asn Pro Ser Asp Ile Pro Asp 790 795 Gln Val Ile Arg Val Phe Lys Val Asp Gln Gln Ser Cys Tyr Ile Ile 805 810 Ile Ser Lys Asp Thr Thr Ala Lys Glu Val Val Phe His Ala Val His

825 830 820 Glu Phe Gly Leu Thr Gly Ala Ser Asp Thr Tyr Ser Leu Cys Glu Val 835 840 Ser Val Thr Pro Glu Gly Val Ile Lys Gln Arg Arg Leu Pro Asp Gln 855 860 Phe Ser Lys Leu Ala Asp Arg Ile Gln Leu Asn Gly Arg Tyr Tyr Leu 870 875 Lys Asn Asn Met Glu Thr Glu Thr Leu Cys Ser Asp Glu Asp Ala Gln 885 890 Glu Leu Val Lys Glu Ser Gln Leu Ser Met Leu Gln Leu Ser Thr Ile 900 905 Glu Val Ala Thr Gln Leu Ser Met Arg Asp Phe Asp Leu Phe Arg Asn 920 Ile Glu Pro Thr Glu Tyr Ile Asp Asp Leu Phe Lys Leu Asn Ser Lys 935 940 Thr Gly Asn Thr His Leu Lys Arg Phe Glu Asp Ile Val Asn Gln Glu 955 950 Thr Phe Trp Val Ala Ser Glu Ile Leu Thr Glu Ala Asn Gln Leu Lys 965 970 Arg Met Lys Ile Ile Lys His Phe Ile Lys Ile Ala Leu His Cys Arg 985 Glu Cys Lys Asn Phe Asn Ser Met Phe Ala Ile Ile Ser Gly Leu Asn 1005 995 1000 Leu Ala Ser Val Ala Arg Leu Arg Gly Thr Trp Glu Lys Leu Pro Ser 1015 1020 Lys Tyr Glu Lys His Leu Gln Asp Leu Gln Asp Ile Phe Asp Pro Ser 1030 1035 Arg Asn Met Ala Lys Tyr Arg Asn Ile Leu Ser Ser Gln Ser Met Gln 1045 1050 1055 Pro Pro Ile Ile Pro Leu Phe Pro Val Val Lys Lys Asp Met Thr Phe 1060 1065 1070 Leu His Glu Gly Asn Asp Ser Lys Val Asp Gly Leu Val Asn Phe Glu 1075 1080 1085 Lys Leu Arg Met Ile Ser Lys Glu Ile Arg Gln Val Val Arg Met Thr 1095 1100 Ser Ala Asn Met Asp Pro Ala Met Met Phe Arg Gln Arg Ser Leu Ser 1110 1115 Gln Gly Ser Thr Asn Ser Asn Met Leu Asp Val Gln Gly Gly Ala His 1125 1130 1135 Lys Lys Arg Ala Arg Arg Ser Ser Leu Leu Asn Ala Lys Lys Leu Tyr 1140 1145 1150 Glu Asp Ala Gln Met Ala Arg Lys Val Lys Gln Tyr Leu Ser Ser Leu 1160 1165 1155 Asp Val Glu Thr Asp Glu Glu Lys Phe Gln Met Met Ser Leu Gln Trp 1175 1180 Glu Pro Ala Tyr Gly Thr Leu Thr Lys Asn Leu Ser Glu Lys Arg Ser 1190 1195 Ala Lys Ser Ser Glu Met Ser Pro Val Pro Met Arg Ser Ala Gly Gln 1205 1210 Thr Thr Lys Ala His Leu His Gln Pro His Arg Val Ser Gln Val Leu 1225 Gln Val Pro Ala Val Asn Leu His Pro Ile Arg Lys Lys Gly Gln Thr 1235 1240 1245 Lys Asp Pro Ala Leu Asn Thr Ser Leu Pro Gln Lys Val Leu Gly Thr 1255 1260 Thr Glu Glu Ile Ser Gly Lys Lys His Thr Glu Asp Thr Ile Ser Val 1270 1275 Ala Ser Ser Leu His Ser Ser Pro Pro Ala Ser Pro Gln Gly Ser Pro 1285 1290 1295 His Lys Gly Tyr Thr Leu Ile Pro Ser Ala Lys Ser Asp Asn Leu Ser 1300 1305

Asp Ser Ser His Ser Glu Ile Ser Ser Arg Ser Ser Ile Val Ser Asn 1315 1320 1325 Cys Ser Val Asp Ser Met Ser Ala Ala Leu Gln Asp Glu Arg Cys Ser 1335 1340 Ser Gln Ala Leu Ala Val Pro Glu Ser Thr Gly Ala Leu Glu Lys Thr 1345 . 1350 1355 1360 Glu His Ala Ser Gly Ile Gly Asp His Ser Gln His Gly Pro Gly Trp 1365 1370 Thr Leu Leu Lys Pro Ser Leu Ile Lys Cys Leu Ala Val Ser Ser Ser 1380 1385 Val Ser Asn Glu Glu Ile Ser Gln Glu His Ile Ile Glu Ala Ala 1395 1400 1405 Asp Ser Gly Arg Gly Ser Trp Thr Ser Cys Ser Ser Ser His Asp 1420 1415 Asn Phe Gln Ser Leu Pro Asn Pro Lys Ser Trp Asp Phe Leu Asn Ser 1425 1430 1435 Tyr Arg His Thr His Leu Asp Asp Pro Ile Ala Glu Val Glu Pro Thr 1445 1450 1455 Asp Ser Glu Pro Tyr Ser Cys Ser Lys Ser Cys Ser Arg Thr Cys Gly 1460 1465 1470 Gln Cys Lys Gly Ser Leu Glu Arg Lys Ser Trp Thr Ser Ser Ser Ser 1475 1480 1485 Leu Ser Asp Thr Tyr Glu Pro Asn Tyr Gly Thr Val Lys Arg Arg Val 1490 1495 1500 Leu Glu Ser Thr Pro Ala Glu Ser Ser Glu Gly Leu Asp Pro Lys Asp 1510 1515 Ala Thr Asp Pro Val Tyr Lys Thr Val Thr Ser Ser Thr Glu Lys Gly 1525 1530 1535 Leu Ile Val Tyr Cys Val Thr Ser Pro Lys Lys Asp Asp Arg Tyr Arg 1540 1545 1550 Glu Pro Pro Pro Thr Pro Pro Gly Tyr Leu Gly Ile Ser Leu Ala Asp 1555 1560 1565 Leu Lys Glu Gly Pro His Thr His Leu Lys Pro Pro Asp Tyr Ser Val 1575 1580 Ala Val Gln Arg Ser Lys Met Met His Asn Ser Leu Ser Arg Leu Pro 1590 1595 Pro Ala Ser Leu Ser Ser Asn Leu Val Ala Cys Val Pro Ser Lys Ile 1605 1610 1615 Val Thr Gln Pro Gln Arg His Asn Leu Gln Pro Phe His Pro Lys Leu 1630 1625 Gly Asp Val Thr Asp Ala Asp Ser Glu Ala Asp Glu Asn Glu Gln Val 1640 Ser Ala Val 1650

<210> 154 <211> 1424 <212> PRT <213> Homo sapiens

<400> 154

 Met
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 Val
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 Ala
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 Asp
 Pro
 Gly

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 Ala
 Trp
 Ala
 Glu
 Leu
 Leu
 Ala
 Gly
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 Lys
 Arg
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 Ala
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 Glu
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 Arg
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 Arg
 Leu
 Leu

55 60 Glu Gly Pro Leu Cys Lys Lys Leu Ser Leu Ser Lys Val Ile Asp Cys 70 75 Asp Ser Ser Glu Ala Tyr Ala Asn His Ser Ser Ser Phe Ile Gly Ser 90 Ala Leu Gln Asp Gln Ala Ser Arg Leu Gly Val Pro Val Gly Ile Leu 105 Ser Ala Gly Met Val Ala Ser Ser Val Gly Gln Ile Cys Thr Ala Pro 120 125 Ala Glu Thr Ser His Pro Val Leu Leu Thr Val Glu Gln Arg Lys Lys 135 140 Leu Ser Ser Leu Leu Glu Phe Ala Gln Tyr Leu Leu Ala His Ser Met 150 155 Phe Ser Arg Leu Ser Phe Cys Gln Glu Leu Trp Lys Ile Gln Ser Ser 170 Leu Leu Glu Ala Val Trp His Leu His Val Gln Gly Ile Val Ser 180 185 Leu Gln Glu Leu Leu Glu Ser His Pro Asp Met His Ala Val Gly Ser 200 Trp Leu Phe Arg Asn Leu Cys Cys Leu Cys Glu Gln Met Glu Ala Ser 215 220 Cys Gln His Ala Asp Val Ala Arg Ala Met Leu Ser Asp Phe Val Gln 230 235 Met Phe Val Leu Arg Gly Phe Gln Lys Asn Ser Asp Leu Arg Arg Thr 245 250 Val Glu Pro Glu Lys Met Pro Gln Val Thr Val Asp Val Leu Gln Arg 265 Met Leu Ile Phe Ala Leu Asp Ala Leu Ala Ala Gly Val Gln Glu Glu 275 280 Ser Ser Thr His Lys Ile Val Arg Cys Trp Phe Gly Val Phe Ser Gly 295 300 His Thr Leu Gly Ser Val Ile Ser Thr Asp Pro Leu Lys Arg Phe Phe 310 315 Ser His Thr Leu Thr Gln Ile Leu Thr His Ser Pro Val Leu Lys Ala 325 330 Ser Asp Ala Val Gln Met Gln Arg Glu Trp Ser Phe Ala Arg Thr His 345 350 Pro Leu Leu Thr Ser Leu Tyr Arg Arg Leu Phe Val Met Leu Ser Ala 360 Glu Glu Leu Val Gly His Leu Gln Glu Val Leu Glu Thr Gln Glu Val 375 His Trp Gln Arg Val Leu Ser Phe Val Ser Ala Leu Val Val Cys Phe 390 395 Pro Glu Ala Gln Gln Leu Leu Glu Asp Trp Val Ala Arg Leu Met Ala 410 Gln Ala Phe Glu Ser Cys Gln Leu Asp Ser Met Val Thr Ala Phe Leu 420 425 Val Val Arg Gln Ala Ala Leu Glu Gly Pro Ser Ala Phe Leu Ser Tyr 440 Ala Asp Trp Phe Lys Ala Ser Phe Gly Ser Thr Arg Gly Tyr His Gly 455 460 Cys Ser Lys Lys Ala Leu Val Phe Leu Phe Thr Phe Leu Ser Glu Leu 470 475 Val Pro Phe Glu Ser Pro Arg Tyr Leu Gln Val His Ile Leu His Pro 485 490 495 Pro Leu Val Pro Ser Lys Tyr Arg Ser Leu Leu Thr Asp Tyr Ile Ser 505 Leu Ala Lys Thr Arg Leu Ala Asp Leu Lys Val Ser Ile Glu Asn Met 520 525 Gly Leu Tyr Glu Asp Leu Ser Ser Ala Gly Asp Ile Thr Glu Pro His 535

Ser Gln Ala Leu Gln Asp Val Glu Lys Ala Ile Met Val Phe Glu His Thr Gly Asn Ile Pro Val Thr Val Met Glu Ala Ser Ile Phe Arg Arg Pro Tyr Tyr Val Ser His Phe Leu Pro Ala Leu Leu Thr Pro Arg Val Leu Pro Lys Val Pro Asp Ser Arg Val Ala Phe Ile Glu Ser Leu Lys Arg Ala Asp Lys Ile Pro Pro Ser Leu Tyr Ser Thr Tyr Cys Gln Ala Cys Ser Ala Ala Glu Glu Lys Pro Glu Asp Ala Ala Leu Gly Val Arg Ala Glu Pro Asn Ser Ala Glu Glu Pro Leu Gly Gln Leu Thr Ala Ala Leu Gly Glu Leu Arg Ala Ser Met Thr Asp Pro Ser Gln Arg Asp Val Ile Ser Ala Gln Val Ala Val Ile Ser Glu Arg Leu Arg Ala Val Leu Gly His Asn Glu Asp Asp Ser Ser Val Glu Ile Ser Lys Ile Gln Leu Ser Ile Asn Thr Pro Arg Leu Glu Pro Arg Glu His Ile Ala Val Asp Leu Leu Leu Thr Ser Phe Cys Gln Asn Leu Met Ala Ala Ser Ser Val Ala Pro Pro Glu Arg Gln Gly Pro Trp Ala Ala Leu Phe Val Arg Thr Met Cys Gly Arg Val Leu Pro Ala Val Leu Thr Arg Leu Cys Gln Leu Leu Arg His Gln Gly Pro Ser Leu Ser Ala Pro His Val Leu Gly Leu Ala Ala Leu Ala Val His Leu Gly Glu Ser Arg Ser Ala Leu Pro Glu Val Asp Val Gly Pro Pro Ala Pro Gly Ala Gly Leu Pro Val Pro Ala Leu Phe Asp Ser Leu Leu Thr Cys Arg Thr Arg Asp Ser Leu Phe Phe Cys Leu Lys Phe Cys Thr Ala Ala Ile Ser Tyr Ser Leu Cys Lys Phe Ser Ser Gln Ser Arg Asp Thr Leu Cys Ser Cys Leu Ser Pro Gly Leu Ile Lys Lys Phe Gln Phe Leu Met Phe Arg Leu Phe Ser Glu Ala Arg Gln Pro Leu Ser Glu Glu Asp Val Ala Ser Leu Ser Trp Arg Pro Leu His Leu Pro Ser Ala Asp Trp Gln Arg Ala Ala Leu Ser Leu Trp Thr His Arg Thr Phe Arg Glu Val Leu Lys Glu Glu Asp Val His Leu Thr Tyr Gln Asp Trp Leu His Leu Glu Leu Glu Ile Gln Pro Glu Ala Asp Ala Leu Ser Asp Thr Glu Arg Gln Asp Phe His Gln Trp Ala Ile His Glu His Phe Leu Pro Glu Ser Ser Ala Ser Gly Gly Cys Asp Gly Asp Leu Gln Ala Ala Cys Thr Ile Leu Val Asn Ala Leu Met Asp Phe His Gln Ser Ser Arg Ser Tyr Asp His Ser Glu Asn Ser Asp Leu Val Phe Gly Gly Arg Thr Gly Asn Glu Asp Ile Ile Ser Arg Leu Gln Glu Met Val Ala Asp Leu Glu Leu Gln Gln Asp Leu Ile Val Pro Leu Gly His

1030 1035 Thr Pro Ser Gln Glu His Phe Leu Phe Glu Ile Phe Arg Arg Leu 1045 1050 1055 Gln Ala Leu Thr Ser Gly Trp Ser Val Ala Ala Ser Leu Gln Arg Gln 1060 1065 Arg Glu Leu Leu Met Tyr Lys Arg Ile Leu Leu Arg Leu Pro Ser Ser 1075 1080 1085 Val Leu Cys Gly Ser Ser Phe Gln Ala Glu Gln Pro Ile Thr Ala Arg 1095 1100 Cys Glu Gln Phe Phe His Leu Val Asn Ser Glu Met Arg Asn Phe Cys 1110 1115 Ser His Gly Gly Ala Leu Thr Gln Asp Ile Thr Ala His Phe Phe Arg 1125 1130 1135 Gly Leu Leu Asn Ala Cys Leu Arg Ser Arg Asp Pro Ser Leu Met Val 1145 1150 1140 Asp Phe Ile Leu Ala Lys Cys Gln Thr Lys Cys Pro Leu Ile Leu Thr 1160 1165 Ser Ala Leu Val Trp Trp Pro Ser Leu Glu Pro Val Leu Leu Cys Arg 1170 1175 1180 Trp Arg Arg His Cys Gln Ser Pro Leu Pro Arg Glu Leu Gln Lys Leu 1190 1195 Gln Glu Gly Arg Gln Phe Ala Ser Asp Phe Leu Ser Pro Glu Ala Ala 1205 1210 1215 Ser Pro Ala Pro Asn Pro Asp Trp Leu Ser Ala Ala Ala Leu His Phe 1220 1225 Ala Ile Gln Gln Val Arg Glu Glu Asn Ile Arg Lys Gln Leu Lys Lys 1235 1240 1245 Leu Asp Cys Glu Arg Glu Glu Leu Leu Val Phe Leu Phe Phe Phe Ser 1260 1255 Leu Met Gly Leu Leu Ser Ser His Leu Thr Ser Asn Ser Thr Thr Asp 1265 1270 1275 Leu Pro Lys Ala Phe His Val Cys Ala Ala Ile Leu Glu Cys Leu Glu 1285 1290 1295 Lys Arg Lys Ile Ser Trp Leu Ala Leu Phe Gln Leu Thr Glu Ser Asp 1300 1305 1310 Leu Arg Leu Gly Arg Leu Leu Arg Val Ala Pro Asp Gln His Thr 1315 1320 Arg Leu Leu Pro Phe Ala Phe Tyr Ser Leu Leu Ser Tyr Phe His Glu 1335 1340 Asp Ala Ala Ile Arg Glu Glu Ala Phe Leu His Val Ala Val Asp Met 1350 1355 Tyr Leu Lys Leu Val Gln Leu Phe Val Ala Gly Asp Thr Ser Thr Val 1365 1370 1375 Ser Pro Pro Ala Gly Arg Ser Leu Glu Leu Lys Gly Gln Ala Gly Gln 1385 Pro Arg Gly Thr Asp Asn Lys Ser Ser Ser Phe Ser Ala Ala Val Asn 1395 1400 1405 Thr Ser Val Pro Glu Lys Glu Leu Leu Thr Arg Gly Arg Ala Ala Gly 1415

<210> 155

<211> 1381

<212> PRT

<213> Homo sapiens

<400> 155

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490 485 Pro Leu Val Pro Ser Lys Tyr Arg Ser Leu Leu Thr Asp Tyr Ile Ser 505 Leu Ala Lys Thr Arg Leu Ala Asp Leu Lys Val Ser Ile Glu Asn Met 520 Gly Leu Tyr Glu Asp Leu Ser Ser Ala Gly Asp Ile Thr Glu Pro His 535 540 Ser Gln Ala Leu Gln Asp Val Glu Lys Ala Ile Met Val Phe Glu His 555 Thr Gly Asn Ile Pro Val Thr Val Met Glu Ala Ser Ile Phe Arg Arg 565 570 Pro Tyr Tyr Val Ser His Phe Leu Pro Ala Leu Leu Thr Pro Arg Val 580 585 Leu Pro Lys Val Pro Asp Ser Arg Val Ala Phe Ile Glu Ser Leu Lys 600 Arg Ala Asp Lys Ile Pro Pro Ser Leu Tyr Ser Thr Tyr Cys Gln Ala Cys Ser Ala Ala Glu Glu Lys Pro Glu Asp Ala Ala Leu Gly Val Arg 630 635 Ala Glu Pro Asn Ser Ala Glu Glu Pro Leu Gly Gln Leu Thr Ala Ala 645 650 Leu Gly Glu Leu Arg Ala Ser Met Thr Asp Pro Ser Gln Arg Asp Val 665 Ile Ser Ala Gln Val Ala Val Ile Ser Glu Arg Leu Arg Ala Val Leu 680 Gly His Asn Glu Asp Asp Ser Ser Val Glu Ile Ser Lys Ile Gln Leu 695 700 Ser Ile Asn Thr Pro Arg Leu Glu Pro Arg Glu His Ile Ala Val Asp 710 715 Leu Leu Leu Thr Ser Phe Cys Gln Asn Leu Met Ala Ala Ser Ser Val 725 730 Ala Pro Pro Glu Arg Gln Gly Pro Trp Ala Ala Leu Phe Val Arg Thr 740 745 Met Cys Gly Arg Val Leu Pro Ala Val Leu Thr Arg Leu Cys Gln Leu 760 Leu Arg His Gln Gly Pro Ser Leu Ser Ala Pro His Val Leu Gly Leu 775 780 Ala Ala Leu Ala Val His Leu Gly Glu Ser Arg Ser Ala Leu Pro Glu 790 795 Val Asp Val Gly Pro Pro Ala Pro Gly Ala Gly Leu Pro Val Pro Ala 805 Leu Phe Asp Ser Leu Leu Thr Cys Arg Thr Arg Asp Ser Leu Phe Phe 825 Cys Leu Lys Phe Cys Thr Ala Ala Ile Ser Tyr Ser Leu Cys Lys Phe 840 Ser Ser Gln Ser Arg Asp Thr Leu Cys Ser Cys Leu Ser Pro Gly Leu 855 860 Ile Lys Lys Phe Gln Phe Leu Met Phe Arg Leu Phe Ser Glu Ala Arg 870 875 Gln Pro Leu Ser Glu Glu Asp Val Ala Ser Leu Ser Trp Arg Pro Leu 885 890 His Leu Pro Ser Ala Asp Trp Gln Arg Ala Ala Leu Ser Leu Trp Thr His Arg Thr Phe Arg Glu Val Leu Lys Glu Glu Asp Val His Leu Thr 915 920 925 Tyr Gln Asp Trp Leu His Leu Glu Leu Glu Ile Gln Pro Glu Ala Asp 935 940 Ala Leu Ser Asp Thr Glu Arg Ser Arg Ser Tyr Asp His Ser Glu Asn 950 955 Ser Asp Leu Val Phe Gly Gly Arg Thr Gly Asn Glu Asp Ile Ile Ser 970

Arg Leu Gln Glu Met Val Ala Asp Leu Glu Leu Gln Gln Asp Leu Ile 980 985 Val Pro Leu Gly His Thr Pro Ser Gln Glu His Phe Leu Phe Glu Ile 1000 - 1005 Phe Arg Arg Arg Leu Gln Ala Leu Thr Ser Gly Trp Ser Val Ala Ala 1015 1020 Ser Leu Gln Arg Gln Arg Glu Leu Leu Met Tyr Lys Arg Ile Leu Leu 1025 1030 1035 Arg Leu Pro Ser Ser Val Leu Cys Gly Ser Ser Phe Gln Ala Glu Gln 1045 1050 1055 Pro Ile Thr Ala Arg Cys Glu Gln Phe Phe His Leu Val Asn Ser Glu 1065 1070 Met Arg Asn Phe Cys Ser His Gly Gly Ala Leu Thr Gln Asp Ile Thr 1075 1080 1085 Ala His Phe Phe Arg Gly Leu Leu Asn Ala Cys Leu Arg Ser Arg Asp 1090 1095 1100 Pro Ser Leu Met Val Asp Phe Ile Leu Ala Lys Cys Gln Thr Lys Cys 1110 1115 1105 Pro Leu Ile Leu Thr Ser Ala Leu Val Trp Trp Pro Ser Leu Glu Pro 1125 , 1130 1135 Val Leu Leu Cys Arg Trp Arg Arg His Cys Gln Ser Pro Leu Pro Arg 1140 1145 Glu Leu Gln Lys Leu Gln Glu Gly Arg Gln Phe Ala Ser Asp Phe Leu 1160 1165 Ser Pro Glu Ala Ala Ser Pro Ala Pro Asn Pro Asp Trp Leu Ser Ala 1175 1180 Ala Ala Leu His Phe Ala Ile Gln Gln Val Arg Glu Glu Asn Ile Arg 1190 1195 Lys Gln Leu Lys Lys Leu Asp Cys Glu Arg Glu Glu Leu Leu Val Phe 1205 1210 1215 Leu Phe Phe Phe Ser Leu Met Gly Leu Leu Ser Ser His Leu Thr Ser 1220 1225 1230 Asn Ser Thr Thr Asp Leu Pro Lys Ala Phe His Val Cys Ala Ala Ile 1235 1240 1245 Leu Glu Cys Leu Glu Lys Arg Lys Ile Ser Trp Leu Ala Leu Phe Gln 1250 1255 1260 Leu Thr Glu Ser Asp Leu Arg Leu Gly Arg Leu Leu Leu Arg Val Ala 1270 1275 Pro Asp Gln His Thr Arg Leu Leu Pro Phe Ala Phe Tyr Ser Leu Leu 1285 1290 1295 Ser Tyr Phe His Glu Asp Ala Ala Ile Arg Glu Glu Ala Phe Leu His 1300 1305 1310 Val Ala Val Asp Met Tyr Leu Lys Leu Val Gln Leu Phe Val Ala Gly 1320 1325 Asp Thr Ser Thr Val Ser Pro Pro Ala Gly Arg Ser Leu Glu Leu Lys 1335 1340 Gly Gln Ala Gly Gln Pro Arg Gly Thr Asp Asn Lys Ser Ser Ser Phe 1350 1355 Ser Ala Ala Val Asn Thr Ser Val Pro Glu Lys Glu Leu Leu Thr Arg 1365 1370 Gly Arg Ala Ala Gly 1380

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      Asn Met Gly Thr Arg Gly Ser Tyr Leu Leu Pro Gly Met Ala

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      240

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      Asp Leu Gln Val Thr Ile Lys Glu
      255
      255

      Glu Ser Asn Pro 246
      Val Pro Tyr Asn Ser Ser Ser Trp Pro Pro Pro Pro Phe Gln Asp
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      Leu Pro Leu Ser Ser Ser Ser Met Thr Pro Ala Ser Ser Ser Ser Ser Arg Pro
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150 155 Leu Gln Pro Asp Asn Ser Thr Leu Thr Trp Val Lys Pro Thr Thr Ala 165 170 Ser Pro Ala Ser Ser Lys Ala Lys Leu Gly Val Leu Asn Asn Thr Ala 185 Glu Pro Gly Lys Phe Pro Leu Leu Gly Asn Ala Gly Leu Ser Ser Leu 200 Thr Glu Gly Val Leu Asp Leu Phe Ala Val Lys Ala Val Tyr Met Gly 215 His Pro Gly Ile Asp Ile His Thr Val Cys Val Gln Asn Lys Leu Gly 230 235 Ser Met Phe Leu Ser Glu Thr Gly Val Thr Leu Leu Tyr Gly Leu Gln 245 250 Thr Thr Asp Asn Arg Leu Leu His Phe Val Ala Pro Lys His Thr Ala 265 Lys Met Leu Phe Ser Gly Leu Leu Glu Leu Thr Arg Ala Val Arg Lys 280 Met Arg Lys Phe Pro Asp Gln Arg Gln Gln Trp Leu Arg Lys Gln Tyr 295 Val Ser Leu Tyr Gln Glu Asp Gly Arg Tyr Glu Gly Pro Thr Leu Ala His Ala Val Glu Leu Phe Gly Gly Arg Arg Trp Ser Ala Arg Asn Pro 330 Ser Pro Gly Thr Ser Ala Lys Asn Ala Glu Lys Pro Asn Met Gln Arg 345 Asn Asn Thr Leu Gly Ile Ser Thr Thr Lys Lys Lys Lys Ile Leu 360 Met Arg Gly Glu Ser Gly Glu Val Thr Asp Asp Glu Met Ala Thr Arg 375 380 Lys Ala Lys Met His Lys Glu Cys Arg Ser Arg Ser Gly Ser Asp Pro 390 395 Gln Asp Ile Asn Glu Glu Glu Ser Glu Val Asn Ala Ile Ala Asn 405 410 Pro Pro Asn Pro Leu Pro Ser Arg Arg Ala His Ser Leu Thr Thr Ala 420 425 Gly Ser Pro Asn Leu Ala Ala Gly Thr Ser Ser Pro Ile Arg Pro Val 440 435 Ser Ser Pro Val Leu Ser Ser Ser Asn Lys Ser Pro Ser Ser Ala Trp 455 460 Ser Ser Ser Trp His Gly Arg Ile Lys Gly Gly Met Lys Gly Phe 470 475 Gln Ser Phe Met Val Ser Asp Ser Asn Met Ser Phe Val Glu Phe Val 490 Glu Leu Phe Lys Ser Phe Ser Val Arg Gln Ala Lys Asp Leu Lys Asp 505 Leu Phe Asp Val Tyr Ala Val Pro Cys Asn Arg Ser Gly Ser Glu Ser 520 Ala Pro Leu Tyr Thr Asn Leu Thr Ile Asp Glu Asn Thr Ser Asp Leu 535 Gln Pro Asp Leu Asp Leu Leu Thr Arg Asn Val Ser Asp Leu Gly Leu 550 555 Phe Ile Lys Ser Lys Gln Gln Leu Ser Asp Asn Gln Arg Gln Ile Ser 570 565 Asp Ala Ile Ala Ala Ser Ile Val Thr Asn Gly Thr Gly Ile Glu 585 Ser Thr Ser Leu Gly Ile Phe Gly Val Gly Ile Leu Gln Leu Asn Asp 600 Phe Leu Val Asn Cys Gln Gly Glu His Cys Thr Tyr Asp Glu Ile Leu 615 620 Ser Ile Ile Gln Lys Phe Glu Pro Ser Ile Ser Met Cys His Gln Gly

Leu Met Ser Phe Glu Gly Phe Ala Arg Phe Leu Met Asp Lys Glu Asn Phe Ala Ser Lys Asn Asp Glu Ser Gln Glu Asn Ile Lys Glu Leu Gln Leu Pro Leu Ser Tyr Tyr Ile Glu Ser Ser His Asn Thr Tyr Leu Thr Gly His Gln Leu Lys Gly Glu Ser Ser Val Glu Leu Tyr Ser Gln Val Leu Leu Gln Gly Cys Arg Ser Val Glu Leu Asp Cys Trp Asp Gly Asp Asp Gly Met Pro Ile Ile Tyr His Gly His Thr Leu Thr Thr Lys Ile Pro Phe Lys Glu Val Val Glu Ala Ile Asp Arg Ser Ala Phe Ile Asn Ser Asp Leu Pro Ile Ile Ile Ser Ile Glu Asn His Cys Ser Leu Pro Gln Gln Arg Lys Met Ala Glu Ile Phe Lys Thr Val Phe Gly Glu Lys Leu Val Thr Lys Phe Leu Phe Glu Thr Asp Phe Ser Asp Asp Pro Met Leu Pro Ser Pro Asp Gln Leu Arg Lys Lys Val Leu Leu Lys Asn Lys Lys Leu Lys Ala His Gln Thr Pro Val Asp Ile Leu Lys Gln Lys Ala His Gln Leu Ala Ser Met Gln Val Gln Ala Tyr Asn Gly Gly Asn Ala Asn Pro Arg Pro Ala Asn Asn Glu Glu Glu Asp Glu Glu Asp Glu Tyr Asp Tyr Asp Tyr Glu Ser Leu Ser Asp Asp Asn Ile Leu Glu Asp Arg Pro Glu Asn Lys Ser Cys Asn Asp Lys Leu Gln Phe Glu Tyr Asn Glu Glu Ile Pro Lys Arg Ile Lys Lys Ala Asp Asn Ser Ala Cys Asn Lys Gly Lys Val Tyr Asp Met Glu Leu Gly Glu Glu Phe Tyr Leu Asp Gln Asn Lys Lys Glu Ser Arg Gln Ile Ala Pro Glu Leu Ser Asp Leu Val Ile Tyr Cys Gln Ala Val Lys Phe Pro Gly Leu Ser Thr Leu Asn Ala Ser Gly Ser Ser Arg Gly Lys Glu Arg Lys Ser Arg Lys Ser Ile Phe Gly Asn Asn Pro Gly Arg Met Ser Pro Gly Glu Thr Ala Ser Phe Asn Lys Thr Ser Gly Lys Ser Ser Cys Glu Gly Ile Arg Gln Thr Trp Glu Glu Ser Ser Ser Pro Leu Asn Pro Thr Thr Ser Leu Ser Ala Ile Ile Arg Thr Pro Lys Cys Tyr His Ile Ser Ser Leu Asn Glu Asn Ala Ala Lys Arg Leu Cys Arg Arg Tyr Ser Gln Lys Leu Thr Gln His Thr Ala Cys Gln Leu Leu Arg Thr Tyr Pro Ala Ala Thr Arg Ile Asp Ser Ser Asn Pro Asn Pro Leu Met Phe Trp Leu His Gly Ile Gln Leu Val Ala Leu Asn Tyr Gln Thr Asp Asp Leu Pro Leu His Leu Asn Ala Ala Met Phe Glu Ala Asn Gly Gly Cys Gly Tyr Val Leu Lys Pro Pro Val Leu Trp Asp Lys Asn Cys Pro Met Tyr Gln Lys Phe Ser Pro Leu

1125 1130 Glu Arg Asp Leu Asp Ser Met Asp Pro Ala Val Tyr Ser Leu Thr Ile 1140 1145 1150 Val Ser Gly Gln Asn Val Cys Pro Ser Asn Ser Met Gly Ser Pro Cys 1155 1160 1165 Ile Glu Val Asp Val Leu Gly Met Pro Leu Asp Ser Cys His Phe Arg 1175 1180 Thr Lys Pro Ile His Arg Asn Thr Leu Asn Pro Met Trp Asn Glu Gln 1190 1195 Phe Leu Phe Arg Val His Phe Glu Asp Leu Val Phe Leu Arg Phe Ala 1205 . 1210 1215 Val Val Glu Asn Asn Ser Ser Ala Val Thr Ala Gln Arg Ile Ile Pro 1220 1225 1230 Leu Lys Ala Leu Lys Arg Gly Tyr Arg His Leu Gln Leu Arg Asn Leu 1235 1240 1245 His Asn Glu Val Leu Glu Ile Ser Ser Leu Phe Ile Asn Ser Arg Arg 1250 1255 1260 Met Glu Glu Asn Ser Ser Gly Asn Thr Met Ser Ala Ser Ser Met Phe 1270 1275 Asn Thr Glu Glu Arg Lys Cys Leu Gln Thr His Arg Val Thr Val His 1285 1290 1295 Gly Val Pro Gly Pro Glu Pro Phe Thr Val Phe Thr Ile Asn Gly Gly 1300 1305 1310 Thr Lys Ala Lys Gln Leu Leu Gln Gln Ile Leu Thr Asn Glu Gln Asp 1315 1320 1325 Ile Lys Pro Val Thr Thr Asp Tyr Phe Leu Met Glu Glu Lys Tyr Phe 1335 1340 Ile Ser Lys Glu Lys Asn Glu Cys Arg Lys Gln Pro Phe Gln Arg Ala 1350 1355 Ile Gly Pro Glu Glu Glu Ile Met Gln Ile Leu Ser Ser Trp Phe Pro 1365 1370 1375 Glu Glu Gly Tyr Met Gly Arg Ile Val Leu Lys Thr Gln Glu Asn 1385 1390 1380 Leu Glu Glu Lys Asn Ile Val Gln Asp Asp Lys Glu Val Ile Leu Ser 1395 1400 1405 Ser Glu Glu Glu Ser Phe Phe Val Gln Val His Asp Val Ser Pro Glu 1410 1415 1420 Gln Pro Arg Thr Val Ile Lys Ala Pro Arg Val Ser Thr Ala Gln Asp 1430 1435 Val Ile Gln Gln Thr Leu Cys Lys Ala Lys Tyr Ser Tyr Ser Ile Leu 1445 1450 1455 Ser Asn Pro Asn Pro Ser Asp Tyr Val Leu Leu Glu Glu Val Val Lys 1460 1465 1470 Asp Thr Thr Asn Lys Lys Thr Thr Thr Pro Lys Ser Ser Gln Arg Val 1480 1485 Leu Leu Asp Gln Glu Cys Val Phe Gln Ala Gln Ser Lys Trp Lys Gly 1495 1500 Ala Gly Lys Phe Ile Leu Lys Leu Lys Glu Gln Val Gln Ala Ser Arg 1510 1515 Glu Asp Lys Lys Cly Ile Ser Phe Ala Ser Glu Leu Lys Lys Leu 1525 1530 1535 Thr Lys Ser Thr Lys Gln Pro Arg Gly Leu Thr Ser Pro Ser Gln Leu **1540 1545 1550** Leu Thr Ser Glu Ser Ile Gln Thr Lys Glu Glu Lys Pro Val Gly Gly 1555 1560 Leu Ser Ser Ser Asp Thr Met Asp Tyr Arg Gln 1575

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405

<210> 165 <211> 407 <212> PRT <213> Homo sapiens

<400> 165 Met Ala Leu Gly Val Gly Arg Ala Arg Pro Gly Leu Ser Cys Gly Val 10 Ile Ser Pro Pro Cys Ala Pro Thr Arg Asn Ser His Pro Gly Pro Gly Cys Thr Ala Ser Pro Pro Ala Pro Pro Gly Trp Pro Phe Ser Gln Arg 40 Gly Pro Gly Arg Trp Ser Thr Thr Glu Leu Arg Lys Glu Lys Ser Arg 55 60 Asp Ala Ala Arg Ser Arg Arg Ser Gln Glu Thr Glu Val Leu Tyr Gln 75 Leu Ala His Thr Leu Pro Phe Ala Arg Gly Val Ser Ala His Leu Asp 85 90 Lys Ala Ser Ile Met Arg Leu Thr Ile Ser Tyr Leu Arg Met His Arg 100 105 Leu Cys Ala Ala Gly Glu Trp Asn Gln Val Gly Ala Gly Gly Glu Pro 120 125 Leu Asp Ala Cys Tyr Leu Lys Ala Leu Glu Gly Phe Val Met Val Leu 135 Thr Ala Glu Gly Asp Met Ala Tyr Leu Ser Glu Asn Val Ser Lys His 150 155 Leu Gly Leu Ser Gln Leu Glu Leu Ile Gly His Ser Ile Phe Asp Phe 165 170 Ile His Pro Cys Asp Gln Glu Glu Leu Gln Asp Ala Leu Thr Pro Gln 185 Gln Thr Leu Ser Arg Arg Lys Val Glu Ala Pro Thr Glu Arg Cys Phe 200 Ser Leu Arg Met Lys Ser Thr Leu Thr Ser Arg Gly Arg Thr Leu Asn 215 220 Leu Lys Ala Ala Thr Trp Lys Val Leu Asn Cys Ser Gly His Met Arg 230 235 Ala Tyr Lys Pro Pro Ala Gln Thr Ser Pro Ala Gly Ser Pro Asp Ser 245 250 255 Glu Pro Pro Leu Gln Cys Leu Val Leu Ile Cys Glu Ala Ile Pro His Pro Gly Ser Leu Glu Pro Pro Leu Gly Arg Gly Ala Phe Leu Ser Arg 280 His Ser Leu Asp Met Lys Phe Thr Tyr Cys Asp Asp Arg Ile Ala Glu 295 300 Val Ala Gly Tyr Ser Pro Asp Asp Leu Ile Gly Cys Ser Ala Tyr Glu 315 Tyr Ile His Ala Leu Asp Ser Asp Ala Val Ser Lys Ser Ile His Thr 325 330 Cys Met Tyr Pro Ile Ser Pro Gly Ala Lys Pro Ala Ala Thr Trp Pro 345 340 Pro Ala Asp Thr Arg Thr Pro Gln Leu Pro Ile Pro Gln Asp Ala Leu 360 Pro Pro His Leu Asn Thr Ser Ser Leu Leu Pro Lys Pro Gln Gly Thr 375 380 Val Ser Phe Leu Ala Pro Ser Tyr Pro Val Pro Arg Ser Phe Ser Pro 390 395 His Leu Pro Pro Trp Pro

320

<210> 166 <211> 418 <212> PRT <213> Homo sapiens

<400> 166 Met Ser Glu Gly Val Asp Leu Ile Asp Ile Tyr Ala Asp Glu Glu Phe Asn Gln Asp Pro Glu Phe Asn Asn Thr Asp Gln Ile Asp Leu Tyr Asp 25 Asp Val Leu Thr Ala Thr Ser Gln Pro Ser Asp Asp Arg Ser Ser 40 Thr Glu Pro Pro Pro Pro Val Arg Gln Glu Pro Ser Pro Lys Pro Asn 55 Asn Lys Thr Pro Ala Ile Leu Tyr Thr Tyr Ser Gly Leu Arg Asn Arg Arg Ala Ala Val Tyr Val Gly Ser Phe Ser Trp Trp Thr Thr Asp Gln 90 Gln Leu Ile Gln Val Ile Arg Ser Ile Gly Val Tyr Asp Val Val Glu 105 Leu Lys Phe Ala Glu Asn Arg Ala Asn Gly Gln Ser Lys Gly Tyr Ala 120 Glu Val Val Ala Ser Glu Asn Ser Val His Lys Leu Leu Glu Leu 135 Leu Pro Gly Lys Val Leu Asn Gly Glu Lys Val Asp Val Arg Pro Ala 150 155 Thr Arg Gln Asn Leu Ser Gln Phe Glu Ala Gln Ala Arg Lys Arg Glu 165 170 175 Cys Val Arg Val Pro Arg Gly Gly Ile Pro Pro Arg Ala His Ser Arg 180 185 Asp Ser Ser Asp Ser Ala Asp Gly Arg Ala Thr Pro Ser Glu Asn Leu 200 Val Pro Ser Ser Ala Arg Val Asp Lys Pro Pro Ser Val Leu Pro Tyr 215 220 Phe Asn Arg Pro Pro Ser Ala Leu Pro Leu Met Gly Leu Pro Pro 230 235 Pro Ile Pro Pro Pro Pro Leu Ser Ser Phe Gly Val Pro Pro 250 245 Pro Pro Pro Gly Ile His Tyr Gln His Leu Met Pro Pro Pro Pro Arg 265 Leu Pro Pro His Leu Ala Val Pro Pro Pro Gly Ala Ile Pro Pro Ala 280 Leu His Leu Asn Pro Ala Phe Leu Pro Pro Pro Asn Ala Thr Val Gly 295 300 Pro Pro Pro Asp Thr Tyr Met Lys Ala Ser Ala Pro Tyr Asn His His 310 315 Gly Ser Arg Asp Ser Gly Pro Pro Pro Ser Thr Val Ser Glu Ala Glu 325 330 335 Phe Glu Asp Ile Met Lys Arg Asn Arg Ala Ile Ser Ser Ser Ala Ile 345 Ser Lys Ala Val Ser Gly Ala Ser Ala Gly Asp Tyr Ser Asp Ala Ile 360 Glu Thr Leu Leu Thr Ala Ile Ala Val Ile Lys Gln Ser Arg Val Ala 375 380 Asn Asp Glu Arg Cys Arg Val Leu Ile Ser Ser Leu Lys Asp Cys Leu 390 395 His Gly Ile Glu Ala Lys Ser Tyr Ser Val Gly Ala Ser Gly Ser Ser 410 Ser Arg

<210> 167 <211> 694 <212> PRT <213> Homo sapiens

<400> 167 Met Gly Ala Pro Ala Cys Ala Leu Ala Leu Cys Val Ala Val Ala Ile 10 Val Ala Gly Ala Ser Ser Glu Ser Leu Gly Thr Glu Gln Arg Val Val 25 Gly Arg Ala Ala Glu Val Pro Gly Pro Glu Pro Gly Gln Gln Glu Gln 40 Leu Val Phe Gly Ser Gly Asp Ala Val Glu Leu Ser Cys Pro Pro Pro 55 60 Gly Gly Gly Pro Met Gly Pro Thr Val Trp Val Lys Asp Gly Thr Gly 75 Leu Val Pro Ser Glu Arg Val Leu Val Gly Pro Gln Arg Leu Gln Val 85 90 Leu Asn Ala Ser His Glu Asp Ser Gly Ala Tyr Ser Cys Arg Gln Arg 105 Leu Thr Gln Arg Val Leu Cys His Phe Ser Val Arg Val Thr Asp Ala 120 Pro Ser Ser Gly Asp Asp Glu Asp Glu Asp Glu Ala Glu Asp Thr 135 140 Gly Val Asp Thr Gly Ala Pro Tyr Trp Thr Arg Pro Glu Arg Met Asp 150 155 Lys Lys Leu Leu Ala Val Pro Ala Ala Asn Thr Val Arg Phe Arg Cys 165 170 Pro Ala Ala Gly Asn Pro Thr Pro Ser Ile Ser Trp Leu Lys Asn Gly 180 185 Arg Glu Phe Arg Gly Glu His Arg Ile Gly Gly Ile Lys Leu Arg His 200 195 Gln Gln Trp Ser Leu Val Met Glu Ser Val Val Pro Ser Asp Arg Gly 215 Asn Tyr Thr Cys Val Val Glu Asn Lys Phe Gly Ser Ile Arg Gln Thr 230 235 240 Tyr Thr Leu Asp Val Leu Glu Arg Ser Pro His Arg Pro Ile Leu Gln 245 250 Ala Gly Leu Pro Ala Asn Gln Thr Ala Val Leu Gly Ser Asp Val Glu 265 Phe His Cys Lys Val Tyr Ser Asp Ala Gln Pro His Ile Gln Trp Leu 280 Lys His Val Glu Val Asn Gly Ser Lys Val Gly Pro Asp Gly Thr Pro 295 Tyr Val Thr Val Leu Lys Val Ser Leu Glu Ser Asn Ala Ser Met Ser 310 315 Ser Asn Thr Pro Leu Val Arg Ile Ala Arg Leu Ser Ser Gly Glu Gly 330 325 Pro Thr Leu Ala Asn Val Ser Glu Leu Glu Leu Pro Ala Asp Pro Lys 340 345 Trp Glu Leu Ser Arg Ala Arg Leu Thr Leu Gly Lys Pro Leu Gly Glu 360 Gly Cys Phe Gly Gln Val Val Met Ala Glu Ala Ile Gly Ile Asp Lys 375 380 Asp Arg Ala Ala Lys Pro Val Thr Val Ala Val Lys Met Leu Lys Asp 390 395

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Asp Ala Thr Asp Lys Asp Leu Ser Asp Leu Val Ser Glu Met Glu Met
               405
                                 410
Met Lys Met Ile Gly Lys His Lys Asn Ile Ile Asn Leu Leu Gly Ala
           420
                              425
Cys Thr Gln Gly Gly Pro Leu Tyr Val Leu Val Glu Tyr Ala Ala Lys
                          440
Gly Asn Leu Arg Glu Phe Leu Arg Ala Arg Arg Pro Pro Gly Leu Asp
                       455
                                          460
Tyr Ser Phe Asp Thr Cys Lys Pro Pro Glu Glu Gln Leu Thr Phe Lys
               470
                                      475
Asp Leu Val Ser Cys Ala Tyr Gln Val Ala Arg Gly Met Glu Tyr Leu
               485
                                  490
                                          495
Ala Ser Gln Lys Cys Ile His Arg Asp Leu Ala Ala Arg Asn Val Leu
                            505
Val Thr Glu Asp Asn Val Met Lys Ile Ala Asp Phe Gly Leu Ala Arg
                          520
Asp Val His Asn Leu Asp Tyr Tyr Lys Lys Thr Thr Asn Gly Arg Leu
                      535
                                       540
Pro Val Lys Trp Met Ala Pro Glu Ala Leu Phe Asp Arg Val Tyr Thr
                   550
                                      555
His Gln Ser Asp Val Trp Ser Phe Gly Val Leu Leu Trp Glu Ile Phe
               565
                                  570
Thr Leu Gly Gly Ser Pro Tyr Pro Gly Ile Pro Val Glu Glu Leu Phe
                              585
                                                 590
Lys Leu Leu Lys Glu Gly His Arg Met Asp Lys Pro Ala Asn Cys Thr
                          600
His Asp Leu Tyr Met Ile Met Arg Glu Cys Trp His Ala Ala Pro Ser
                      615
                                        620
Gln Arg Pro Thr Phe Lys Gln Leu Val Glu Asp Leu Asp Arg Val Leu
                  630
                                     635
Thr Val Thr Ser Thr Asp Glu Tyr Leu Asp Leu Ser Ala Pro Phe Glu
               645
                                  650
Gln Tyr Ser Pro Gly Gly Gln Asp Thr Pro Ser Ser Ser Ser Gly
                              665
                                                 670
Asp Asp Ser Val Phe Ala His Asp Leu Leu Pro Pro Ala Pro Pro Ser
      675
                          680
                                             685
Ser Gly Gly Ser Arg Thr
   690
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<210> 168 <211> 53

<212> PRT

<213> Homo sapiens

Cys Gly Tyr Lys Gly 50

<210> 169 <211> 42

<212> PRT <213> Homo sapiens

<210> 170 <211> 289 <212> PRT <213> Homo sapiens

<400> 170 Met Phe Val Leu Tyr Val Thr Ser Phe Ala Ile Cys Ala Ser Gly 10 Gln Pro Arg Gly Asn Gln Leu Lys Gly Glu Asn Tyr Ser Pro Arg Tyr Ile Cys Ser Ile Pro Gly Leu Pro Gly Pro Pro Gly Pro Pro Gly Ala 40 Asn Gly Ser Pro Gly Pro His Gly Arg Ile Gly Leu Pro Gly Arg Asp 55 Gly Arg Asp Gly Arg Lys Gly Glu Lys Gly Glu Lys Gly Thr Ala Gly Leu Arg Gly Lys Thr Gly Pro Leu Gly Leu Ala Gly Glu Lys Gly Asp Gln Gly Glu Thr Gly Lys Lys Gly Pro Ile Gly Pro Glu Gly Glu Lys 100 105 Gly Glu Val Gly Pro Ile Gly Pro Pro Gly Pro Lys Gly Asp Arg Gly 120 Glu Gln Gly Asp Pro Gly Leu Pro Gly Val Cys Arg Cys Gly Ser Ile 135 140 Val Leu Lys Ser Ala Phe Ser Val Gly Ile Thr Thr Ser Tyr Pro Glu 150 155 Glu Arg Leu Pro Ile Ile Phe Asn Lys Val Leu Phe Asn Glu Gly Glu 170 His Tyr Asn Pro Ala Thr Gly Lys Phe Ile Cys Ala Phe Pro Gly Ile 185 Tyr Tyr Phe Ser Tyr Asp Ile Thr Leu Ala Asn Lys His Leu Ala Ile 200 Gly Leu Val His Asn Gly Gln Tyr Arg Ile Lys Thr Phe Asp Ala Asn 215 Thr Gly Asn His Asp Val Ala Ser Gly Ser Thr Val Ile Tyr Leu Gln 230 235 Pro Glu Asp Glu Val Trp Leu Glu Ile Phe Phe Thr Asp Gln Asn Gly 250 245 Leu Phe Ser Asp Pro Gly Trp Ala Asp Ser Leu Phe Ser Gly Phe Leu 265 Leu Tyr Val Asp Thr Asp Tyr Leu Asp Ser Ile Ser Glu Asp Asp Glu 280 Leu

<210> 171 <211> 170 <212> PRT <213> Homo sapiens

<400> 171 Met Asp Ala Leu Ser Glu Ala Asn Gly Thr Phe Ala Leu Asn Leu Leu 10 Lys Lys Leu Gly Glu Asn Asn Ser Asn Asn Leu Phe Phe Ser Pro Leu 25 Ser Ile Ser Ser Ala Leu Ala Met Val Phe Met Gly Ala Lys Gly Asn 40 Thr Ala Ala Gln Met Ser Gln Ala Leu Cys Phe Ser Lys Ile Gly Gly 55 Glu Asp Gly Asp Ile His Arg Gly Phe Gln Ser Leu Leu Val Ala Ile 70 75 Asn Arg Thr Asp Thr Glu Tyr Val Leu Arg Thr Ala Asn Gly Leu Phe 90 Gly Glu Lys Ser Tyr Asp Phe Leu Thr Gly Phe Thr Asp Ser Cys Gly 105 Lys Phe Tyr Gln Ala Thr Ile Lys Gln Leu Asp Phe Val Asn Asp; Thr . 115 120 Glu Lys Ser Thr Thr Arg Val Asn Ser Trp Val Ala Asp Lys Thr Lys 135 140 Gly Glu Asn Ile Leu Leu Phe Tyr Phe Asp Asn Ile Leu Asn Ser Phe 150 Ile Val Ser Ser Leu Gln Asn Cys Gln Ile

<210> 172 <211> 212 <212> PRT <213> Homo sapiens

<400> 172 Met Leu Ser Ser Val Val Phe Trp Gly Leu Ile Ala Leu Ile Gly Thr 10 Ser Arg Gly Ser Tyr Pro Phe Ser His Ser Met Lys Pro His Leu His 25 Pro Arg Leu Tyr His Gly Cys Tyr Gly Asp Ile Met Thr Met Lys Thr 40 Ser Gly Ala Thr Cys Asp Ala Asn Ser Val Met Asn Cys Gly Ile Arg 55 60 Gly Ser Glu Met Phe Ala Glu Met Asp Leu Arg Ala Ile Lys Pro Tyr 70 75 Gln Thr Leu Ile Lys Glu Val Gly Gln Arg His Cys Val Asp Pro Ala 85 90 Val Ile Ala Ala Ile Ile Ser Arg Glu Ser His Gly Gly Ser Val Leu 105 Gln Asp Gly Trp Asp His Arg Gly Leu Lys Phe Gly Leu Met Gln Leu 120 Asp Lys Gln Thr Tyr His Pro Val Gly Ala Trp Asp Ser Lys Glu His 135 140 Leu Ser Gln Ala Thr Gly Ile Leu Thr Glu Arg Ile Lys Ala Ile Gln 150 155 Lys Lys Phe Pro Thr Trp Ser Val Ala Gln His Leu Lys Gly Gly Leu

<210> 173 <211> 581 <212> PRT <213> Homo sapiens

<400> 173 Met Val Phe Arg Asn Val Gly Arg Pro Pro Glu Glu Asp Val Glu Ala Ala Pro Glu Pro Gly Pro Ser Glu Leu Leu Cys Pro Arg His Arg 20 25 Cys Ala Leu Asp Pro Lys Ala Leu Pro Pro Gly Leu Ala Leu Glu Arg 40 Thr Trp Gly Pro Ala Ala Gly Leu Glu Ala Gln Leu Ala Ala Leu Gly 55 Leu Gly Gln Pro Ala Gly Pro Gly Val Lys Thr Val Gly Gly Gly Cys 70 75 Cys Pro Cys Pro Cys Pro Pro Gln Pro Pro Pro Gln Pro Gln Pro 90 Pro Ala Ala Ala Pro Gln Ala Gly Glu Asp Pro Thr Glu Thr Ser Asp 105 Ala Leu Leu Val Leu Glu Gly Leu Glu Ser Glu Ala Glu Ser Leu Glu 115 120 125 Thr Asn Ser Cys Ser Glu Glu Glu Leu Ser Ser Pro Gly Arg Gly Gly 135 140 Gly Gly Gly Arg Leu Leu Gln Pro Pro Gly Pro Glu Leu Pro 150 155 Pro Val Pro Phe Pro Leu Gln Asp Leu Val Pro Leu Gly Arg Leu Ser 165 170 Arg Gly Glu Gln Gln Gln Gln Gln Gln Pro Pro Pro Pro 185 Pro Pro Pro Gly Pro Leu Arg Pro Leu Ala Gly Pro Ser Arg Lys Gly 200 Ser Phe Lys Ile Arg Leu Ser Arg Leu Phe Arg Thr Lys Ser Cys Asn 215 220 Gly Gly Ser Gly Gly Asp Gly Thr Gly Lys Arg Pro Ser Gly Glu 230 235 Leu Ala Ala Ser Ala Ala Ser Leu Thr Asp Met Gly Gly Ser Ala Gly 245 250 Arg Glu Leu Asp Ala Gly Arg Lys Pro Lys Leu Thr Arg Thr Gln Ser 265 270 Ala Phe Ser Pro Val Ser Phe Ser Pro Leu Phe Thr Gly Glu Thr Val 275 280 285 Ser Leu Val Asp Val Asp Ile Ser Gln Arg Gly Leu Thr Ser Pro His 295 300 Pro Pro Pro Pro Pro Pro Arg Arg Ser Leu Ser Leu Leu Asp 310 315 Asp Ile Ser Gly Thr Leu Pro Thr Ser Val Leu Val Ala Pro Met Gly 325 330 Ser Ser Leu Gln Ser Phe Pro Leu Pro Pro Pro Pro Pro Pro His Ala 340 345

Pro Asp Ala Phe Pro Arg Ile Ala Pro Ile Arg Ala Ala Glu Ser Leu 36Ó His Ser Gln Pro Pro Gln His Leu Gln Cys Pro Leu Tyr Arg Pro Asp 375 380 Ser Ser Ser Phe Ala Ala Ser Leu Arg Glu Leu Glu Lys Cys Gly Trp 390 395 Tyr Trp Gly Pro Met Asn Trp Glu Asp Ala Glu Met Lys Leu Lys Gly 410 405 Lys Pro Asp Gly Ser Phe Leu Val Arg Asp Ser Ser Asp Pro Arg Tyr 420 425 Ile Leu Ser Leu Ser Phe Arg Ser Gln Gly Ile Thr His His Thr Arg 435 440 Met Glu His Tyr Arg Gly Thr Phe Ser Leu Trp Cys His Pro Lys Phe 455 460 Glu Asp Arg Cys Gln Ser Val Val Glu Phe Ile Lys Arg Ala Ile Met 470 475 His Ser Lys Asn Gly Lys Phe Leu Tyr Phe Leu Arg Ser Arg Val Pro 485 490 Gly Leu Pro Pro Thr Pro Val Gln Leu Leu Tyr Pro Val Ser Arg Phe 500 505 Ser Asn Val Lys Ser Leu Gln His Leu Cys Arg Phe Arg Ile Arg Gln 520 525 Leu Val Arg Ile Asp His Ile Pro Asp Leu Pro Leu Pro Lys Pro Leu 535 Ile Ser Tyr Ile Arg Lys Phe Tyr Tyr Tyr Asp Pro Gln Glu Glu Val 550 555 Tyr Leu Ser Leu Lys Glu Ala Gln Leu Ile Ser Lys Gln Lys Gln Glu 565 570 Val Glu Pro Ser Thr 580

<210> 174 <211> 87 <212> PRT <213> Homo sapiens

<210> 175 <211> 193 <212> PRT <213> Homo sapiens

<400> 175 Met Leu Arg Cys Gly Leu Ala Cys Glu Arg Cys Arg Trp Ile Leu Pro Leu Leu Leu Ser Ala Ile Ala Phe Asp Ile Ile Ala Leu Ala Gly Arg Gly Trp Leu Gln Ser Ser Asn His Ile Gln Thr Ser Ser Leu Trp 40 Trp Arg Cys Phe Asp Glu Gly Gly Ser Gly Ser Tyr Asp Asp Gly 55 Cys Gln Ser Leu Met Glu Tyr Ala Trp Gly Arg Ala Ala Ala Thr 70 Leu Phe Cys Gly Phe Ile Ile Leu Cys Ile Cys Phe Ile Leu Ser Phe 85 90 Phe Ala Leu Cys Gly Pro Gln Met Leu Val Phe Leu Arg Val Ile Gly 105 Gly Leu Leu Ala Leu Ala Ala Ile Phe Gln Ile Ile Ser Leu Val Ile 120 Tyr Pro Val Lys Tyr Thr Gln Thr Phe Thr Leu His Asp Asn Pro Ala 135 Val Asn Tyr Ile Tyr Asn Trp Ala Tyr Gly Phe Gly Trp Ala Ala Thr 155 150 Ile Ile Leu Ile Gly Cys Ser Phe Phe Phe Cys Cys Leu Pro Asn Tyr . 170 165 Glu Asp Asp Leu Leu Gly Ala Ala Lys Pro Arg Tyr Phe Tyr Pro Pro 185 Ala

<210> 176 <211> 87 <212> PRT <213> Homo sapiens

<400> 176 Met Gly Leu Met Phe Leu Pro Cys Leu Ile Asn Leu Phe Gln Arg Phe 10 5 Phe Lys Leu Thr Gly Ser Trp Pro Phe His Arg Gln Leu Pro Lys Asn 25 20 Ile Tyr Arg Arg His Cys Ser Tyr Gln His Asp Thr Arg Glu Leu Ser 40 Val Pro Ser Ser Ala Gly Ser Ser Gln Lys Glu His Ala Ala Pro Arg 55 Pro Phe Tyr Asn Tyr Glu Val Trp Ile Asp Arg Ala Glu Ala Ser Pro 70 75 Leu Trp Ile Ser Ala Ser Phe 85

<210> 177 <211> 83 <212> PRT <213> Homo sapiens

<400> 177
Met Ser Leu Leu Arg Leu His Arg Leu Ser Ile Ile Trp Lys Asn Leu
1 5 10 15

 Ile
 Phe
 His
 Gln
 Glu
 Tyr
 Glu
 His
 Val
 Phe
 Gln
 Val
 Glu
 Asn
 Ala
 Lys

 Asp
 Asn
 Glu
 Asp
 Ser
 Ile
 Leu
 Gln
 Arg
 Glu
 Ile
 Pro
 Ala
 Arg
 Gln
 Ser

 Arg
 Arg
 Arg
 Phe
 Arg
 Lys
 Ile
 Asn
 Tyr
 Lys
 Gly
 Glu
 Arg
 Gln
 Thr
 Ile

 Asn
 Asp
 Val
 Glu
 Val
 Asn
 Ser
 Tyr
 Leu
 Ser
 Val
 Ser
 Ile
 Phe
 Arg

 Asn
 Thr
 Ser
 Ser
 Tyr
 Leu
 Ser
 Val
 Ser
 Ile
 Phe
 Arg

 Asn
 Thr
 Ser
 Ser
 Tyr
 Leu
 Ser
 Val
 Ser
 Ile
 Phe
 Arg

 Asn
 Thr
 Ser
 Tyr
 Leu
 Ser
 Val
 Ser
 Ile
 Phe
 Arg

 Asn
 T

<210> 178 <211> 662 <212> PRT <213> Homo sapiens

<400> 178 Met Lys Glu Val Thr Phe His Cys His Glu Gly Tyr Ile Leu His Gly 1.0 Ala Pro Lys Leu Thr Cys Gln Ser Asp Gly Asn Trp Asp Ala Glu Ile Pro Leu Cys Lys Pro Val Asn Cys Gly Pro Pro Glu Asp Leu Ala His 35 40 Gly Phe Pro Asn Gly Phe Ser Phe Ile His Gly Gly His Ile Gln Tyr 55 Gln Cys Phe Pro Gly Tyr Lys Leu His Gly Asn Ser Ser Arg Arg Cys 75 Leu Ser Asn Gly Ser Trp Ser Gly Ser Ser Pro Ser Cys Leu Pro Cys 85 90 Arg Cys Ser Thr Pro Val Ile Glu Tyr Gly Thr Val Asn Gly Thr Asp 100 105 Phe Asp Cys Gly Lys Ala Ala Arg Ile Gln Cys Phe Lys Gly Phe Lys 120 Leu Leu Gly Leu Ser Glu Ile Thr Cys Glu Ala Asp Gly Gln Trp Ser - 135 140 Ser Gly Phe His His Phe Glu His Thr Ser Cys Gly Ser Leu Pro Met 150 155 Ile Pro Asn Ala Phe Ile Ser Glu Thr Ser Ser Trp Lys Glu Asn Val 170 Ile Thr Tyr Ser Cys Arg Ser Gly Tyr Val Ile Gln Gly Ser Ser Asp 180 185 Leu Ile Cys Thr Glu Lys Gly Val Trp Ser Gln Pro Tyr Pro Val Cys 195 200 205 Glu Pro Leu Ser Cys Gly Ser Pro Pro Ser Val Ala Asn Ala Val Ala 215 220 Thr Gly Glu Ala His Thr Tyr Glu Ser Glu Val Lys Leu Arg Cys Leu 230 Glu Gly Tyr Thr Met Asp Thr Asp Thr Arg Ser Ile Thr Cys Gln Lys 245 250 Asp Gly Arg Trp Phe Pro Glu Arg Ile Ser Cys Ser Pro Lys Lys Cys 265 270 Pro Leu Pro Glu Asn Ile Thr His Ile Leu Val His Gly Asp Asp Phe 275 280 285 Ser Val Asn Arg Gln Val Ser Val Ser Cys Ala Glu Gly Tyr Thr Phe 295 300 Glu Gly Val Asn Ile Ser Val Cys Gln Leu Asp Gly Thr Trp Glu Pro 310 315 Pro Phe Ser Asp Glu Ser Cys Ser Pro Val Ser Cys Gly Lys Pro Glu

325 330 Ser Pro Glu His Gly Phe Val Val Gly Ser Lys Tyr Thr Phe Glu Ser 345 Thr Ile Ile Tyr Gln Cys Glu Pro Gly Tyr Glu Leu Glu Gly Asn Arg 360 Glu Arg Val Cys Gln Glu Asn Arg Gln Trp Ser Gly Gly Val Ala Ile 375 380 Cys Lys Glu Thr Arg Cys Glu Thr Pro Leu Glu Phe Leu Asn Gly Lys 390 395 Ala Asp Ile Glu Asn Arg Thr Thr Gly Pro Asn Val Val Tyr Ser Cys 410 Asn Arg Gly Tyr Ser Leu Glu Gly Pro Ser Glu Ala His Cys Thr Glu 420 425 Asn Gly Thr Trp Ser His Pro Val Pro Leu Cys Lys Pro Asn Pro Cys 440 Pro Val Pro Phe Val Ile Pro Glu Asn Ala Leu Leu Ser Glu Lys Glu 455 Phe Tyr Val Asp Gln Asn Val Ser Ile Lys Cys Arg Glu Gly Phe Leu 470 475 Leu Gln Gly His Gly Ile Ile Thr Cys Asn Pro Asp Glu Thr Trp Thr 485 490 495 Gln Thr Ser Ala Lys Cys Glu Lys Ile Ser Cys Gly Pro Pro Ala His 505 Val Glu Asn Ala Ile Ala Arg Gly Val His Tyr Gln Tyr Gly Asp Met 520 Ile Thr Tyr Ser Cys Tyr Ser Gly Tyr Met Leu Glu Gly Phe Leu Arg 535 540 Ser Val Cys Leu Glu Asn Gly Thr Trp Thr Ser Pro Pro Ile Cys Arg 550 555 Ala Val Cys Arg Phe Pro Cys Gln Asn Gly Gly Ile Cys Gln Arg Pro 565 570 Asn Ala Cys Ser Cys Pro Glu Gly Trp Met Gly Arg Leu Cys Glu Glu 585 Leu Ile Cys Ile Leu Pro Cys Leu Asn Gly Gly Arg Cys Val Ala Pro 600 Tyr Gln Cys Asp Cys Pro Pro Gly Trp Thr Gly Ser Arg Cys His Thr 615 Ala Val Cys Gln Ser Pro Cys Leu Asn Gly Gly Lys Cys Val Arg Pro 630 635 Asn Arg Cys His Cys Leu Ser Ser Trp Thr Gly His Asn Cys Ser Arg 645 Lys Arg Arg Thr Gly Phe 660

<210> 179 <211> 1867 <212> PRT <213> Homo sapiens

Phe Phe Val Ala Val Leu Thr Asp Ile Asn Ser Glu Arg His Tyr Cys 70 75 Ala Cys Leu Thr Phe Trp Glu Pro Ala Glu Pro Ser Gln Glu Thr Thr 85 90 Arg Val Glu Asp Ala Thr Glu Arg Glu Glu Glu Gly Asp Glu Gly Gly 105 Gln Thr His Leu Ser Pro Thr Ala Pro Ala Pro Ser Ala Gln Leu Phe 120 Ala Pro Lys Thr Leu Val Leu Val Ser Arg Leu Asp His Thr Glu Val 135 Phe Arg Asn Ser Leu Gly Leu Ile Tyr Ala Ile His Val Glu Gly Leu 150 155 Asn Val Cys Leu Glu Asn Val Ile Gly Asn Leu Leu Thr Cys Thr Val 165 170 Pro Leu Ala Gly Gly Ser Gln Arg Thr Ile Ser Leu Gly Ala Gly Asp 185 Arg Gln Val Ile Gln Thr Pro Leu Ala Asp Ser Leu Pro Val Ser Arg 195 200 Cys Ser Val Ala Leu Leu Phe Arg Gln Leu Gly Ile Thr Asn Val Leu 215 220 Ser Leu Phe Cys Ala Ala Leu Thr Glu His Lys Val Leu Phe Leu Ser 235 Arg Ser Tyr Gln Arg Leu Ala Asp Ala Cys Arg Gly Leu Leu Ala Leu 245 250 Leu Phe Pro Leu Arg Tyr Ser Phe Thr Tyr Val Pro Ile Leu Pro Ala 265 Gln Leu Leu Glu Val Leu Ser Thr Pro Thr Pro Phe Ile Ile Gly Val 280 Asn Ala Ala Phe Gln Ala Glu Thr Gln Glu Leu Leu Asp Val Ile Val 295 300 Ala Asp Leu Asp Gly Gly Thr Val Thr Ile Pro Glu Cys Val His Ile 310 315 Pro Pro Leu Pro Glu Pro Leu Gln Ser Gln Thr His Ser Val Leu Ser 325 330 Met Val Leu Asp Pro Glu Leu Glu Leu Ala Asp Leu Ala Phe Pro Pro 340 345 Pro Thr Thr Ser Thr Ser Ser Leu Lys Met Gln Asp Lys Glu Leu Arg 360 Ala Val Phe Leu Arg Leu Phe Ala Gln Leu Leu Gln Gly Tyr Arg Trp 375 380 Cys Leu His Val Val Arg Ile His Pro Glu Pro Val Ile Arg Phe His 390 395 Lys Ala Ala Phe Leu Gly Gln Arg Gly Leu Val Glu Asp Asp Phe Leu 410 Met Lys Val Leu Glu Gly Met Ala Phe Ala Gly Phe Val Ser Glu Arg 420 425 Gly Val Pro Tyr Arg Pro Thr Asp Leu Phe Asp Glu Leu Val Ala His 440 Glu Val Ala Arg Met Arg Ala Asp Glu Asn His Pro Gln Arg Val Leu 455 460 Arg His Val Gln Glu Leu Ala Glu Gln Leu Tyr Lys Asn Glu Asn Pro 470 475 Tyr Pro Ala Val Ala Met His Lys Val Gln Arg Pro Gly Glu Ser Ser 485 490 His Leu Arg Arg Val Pro Arg Pro Phe Pro Arg Leu Asp Glu Gly Thr 505 Val Gln Trp Ile Val Asp Gln Ala Ala Ala Lys Met Gln Gly Ala Pro 515 520 525 Pro Ala Val Lys Ala Glu Arg Arg Thr Thr Val Pro Ser Gly Pro Pro 535 540 Met Thr Ala Ile Leu Glu Arg Cys Ser Gly Leu His Val Asn Ser Ala

Arg Arg Leu Glu Val Val Arg Asn Cys Ile Ser Tyr Val Phe Glu Gly Lys Met Leu Glu Ala Lys Lys Leu Leu Pro Ala Val Leu Arg Ala Leu Lys Gly Arg Val Ala Arg Arg Cys Leu Ala Gln Glu Leu His Leu His Val Gln Gln Asn Arg Ala Val Leu Asp His Gln Gln Phe Asp Phe Val Val Arg Met Met Asn Cys Cys Leu Gln Asp Cys Thr Ser Leu Asp Glu His Gly Ile Ala Ala Leu Leu Pro Leu Val Thr Ala Phe Cys Arg Lys Leu Ser Pro Gly Val Thr Gln Phe Ala Tyr Ser Cys Val Gln Glu His Val Val Trp Ser Thr Pro Gln Phe Trp Glu Ala Met Phe Tyr Gly Asp Val Gln Thr His Ile Arg Ala Leu Tyr Leu Glu Pro Thr Glu Asp Leu Ala Pro Ala Gln Glu Val Gly Glu Ala Pro Ser Gln Glu Asp Glu Arg Ser Ala Leu Asp Val Ala Ser Glu Gln Arg Arg Leu Trp Pro Thr Leu Ser Arg Glu Lys Gln Gln Glu Leu Val Gln Lys Glu Glu Ser Thr Val Phe Ser Gln Ala Ile His Tyr Ala Asn Arg Met Ser Tyr Leu Leu Leu Pro Leu Asp Ser Ser Lys Ser Arg Leu Leu Arg Glu Arg Ala Gly Leu Gly Asp Leu Glu Ser Ala Ser Asn Ser Leu Val Thr Asn Ser Met Ala Gly Ser Val Ala Glu Ser Tyr Asp Thr Glu Ser Gly Phe Glu Asp Ala Glu Thr Cys Asp Val Ala Gly Ala Val Val Arg Phe Ile Asn Arg Phe Val Asp Lys Val Cys Thr Glu Ser Gly Val Thr Ser Asp His Leu Lys Gly Leu His Val Met Val Pro Asp Ile Val Gln Met His Ile Glu Thr Leu Glu Ala Val Gln Arg Glu Ser Arg Arg Leu Pro Pro Ile Gln Lys Pro Lys Leu Leu Arg Pro Arg Leu Leu Pro Gly Glu Glu Cys Val Leu Asp Gly Leu Arg Val Tyr Leu Leu Pro Asp Gly Arg Glu Gly Ala Gly Gly Ser Ala Gly Gly Pro Ala Leu Leu Pro Ala Glu Gly Ala Val Phe Leu Thr Thr Tyr Arg Val Ile Phe Thr Gly Met Pro Thr Asp Pro Leu Val Gly Glu Gln Val Val Val Arg Ser Phe Pro Val Ala Ala Leu Thr Lys Glu Lys Arg Ile Ser Val Gln Thr Pro Val Asp Gln Leu Leu Gln Asp Gly Leu Gln Leu Arg Ser Cys Thr Phe Gln Leu Leu Lys Met Ala Phe Asp Glu Glu Val Gly Ser Asp Ser Ala Glu Leu Phe Arg Lys Gln Leu His Lys Leu Arg Tyr Pro Pro Asp Ile Arg Ala Thr Phe Ala Phe Thr Leu Gly Ser Ala His Thr Pro Gly Arg Pro Pro Arg Val

Thr Lys Asp Lys Gly Pro Ser Leu Arg Thr Leu Ser Arg Asn Leu Val 1050 Lys Asn Ala Lys Lys Thr Ile Gly Arg Gln His Val Thr Arg Lys Lys 1065 1060 1070 Tyr Asn Pro Pro Ser Trp Glu His Arg Gly Gln Pro Pro Pro Glu Asp 1080 Gln Glu Asp Glu Ile Ser Val Ser Glu Glu Leu Glu Pro Ser Thr Leu 1095 1100 Thr Pro Ser Ser Ala Leu Lys Pro Ser Asp Arg Met Thr Met Ser Ser 1110 1115 Leu Val Glu Arg Ala Cys Cys Arg Asp Tyr Gln Arg Leu Gly Leu Gly 1125 1130 Thr Leu Ser Ser Ser Leu Ser Arg Ala Lys Ser Glu Pro Phe Arg Ile 1140 1145 1150 Ser Pro Val Asn Arg Met Tyr Ala Ile Cys Arg Ser Tyr Pro Gly Leu 1160 1165 Leu Ile Val Arg Gln Ser Val Gln Asp Asn Ala Leu Gln Arg Val Ser 1170 1175 1180 Arg Cys Tyr Arg Gln Asn Arg Phe Pro Val Val Cys Trp Arg Ser Gly 1190 1195 Arg Ser Lys Ala Val Leu Leu Arg Ser Gly Gly Leu His Gly Lys Gly 1205 1210 1215 Val Val Gly Leu Phe Lys Ala Gln Asn Ala Pro Ser Pro Gly Gln Ser 1220 1225 1230 Gln Ala Asp Ser Ser Leu Glu Gln Glu Lys Tyr Leu Gln Ala Val 1235 1240 1245 Val Ser Ser Met Pro Arg Tyr Ala Asp Ala Ser Gly Arg Asn Thr Leu 1250 1255 1260 Ser Gly Phe Ser Ser Ala His Met Gly Ser His Gly Lys Trp Gly Ser 1270 1275 Val Arg Thr Ser Gly Arg Ser Ser Gly Leu Gly Thr Asp Val Gly Ser 1285 1290 Arg Leu Ala Gly Arg Asp Ala Leu Ala Pro Pro Gln Ala Asn Gly Gly 1300 1305 Pro Pro Asp Pro Gly Phe Leu Arg Pro Gln Arg Ala Ala Leu Tyr Ile 1320 1325 Leu Gly Asp Lys Ala Gln Leu Lys Gly Val Arg Ser Asp Pro Leu Gln 1330 1335 1340 Gln Trp Glu Leu Val Pro Ile Glu Val Phe Glu Ala Arg Gln Val Lys 1350 1355 Ala Ser Phe Lys Lys Leu Leu Lys Ala Cys Val Pro Gly Cys Pro Ala 1365 1370 Ala Glu Pro Ser Pro Ala Ser Phe Leu Arg Ser Leu Glu Asp Ser Glu 1380 1385 Trp Leu Ile Gln Ile His Lys Leu Leu Gln Val Ser Val Leu Val Val 1395 1400 1405 Glu Leu Leu Asp Ser Gly Ser Ser Val Leu Val Gly Leu Glu Asp Gly 1415 1420 Trp Asp Ile Thr Thr Gln Val Val Ser Leu Val Gln Leu Leu Ser Asp 1430 1435 Pro Phe Tyr Arg Thr Leu Glu Gly Phe Arg Leu Leu Val Glu Lys Glu 1445 1450 1455 Trp Leu Ser Phe Gly His Arg Phe Ser His Arg Gly Ala His Thr Leu 1465 1470 Ala Gly Gln Ser Ser Gly Phe Thr Pro Val Phe Leu Gln Phe Leu Asp 1475 1480 1485 Cys Val His Gln Val His Leu Gln Phe Pro Met Glu Phe Glu Phe Ser 1495 1500 Gln Phe Tyr Leu Lys Phe Leu Gly Tyr His His Val Ser Arg Arg Phe 1510 1515 Arg Thr Phe Leu Leu Asp Ser Asp Tyr Glu Arg Ile Glu Leu Gly Leu

1525 1530 Leu Tyr Glu Glu Lys Gly Glu Arg Arg Gly Gln Val Pro Cys Arg Ser 1545 1540 Val Trp Glu Tyr Val Asp Arg Leu Ser Lys Arg Thr Pro Val Phe His 1555 1560 1565 Asn Tyr Met Tyr Ala Pro Glu Asp Ala Glu Val Leu Arg Pro Tyr Ser 1575 1580 Asn Val Ser Asn Leu Lys Val Trp Asp Phe Tyr Thr Glu Glu Thr Leu 1590 1595 Ala Glu Gly Pro Pro Tyr Asp Trp Glu Leu Ala Gln Gly Pro Pro Glu 1605 1610 1615 Pro Pro Glu Glu Glu Arg Ser Asp Gly Gly Ala Pro Gln Ser Arg Arg 1620 1625 1630 Arg Val Val Trp Pro Cys Tyr Asp Ser Cys Pro Arg Ala Gln Pro Asp 1640 1645 Ala Ile Ser Arg Leu Leu Glu Glu Leu Gln Arg Leu Glu Thr Glu Leu 1655 1660 Gly Gln Pro Ala Glu Arg Trp Lys Asp Thr Trp Asp Arg Val Lys Ala 1670 1675 Ala Gln Arg Leu Glu Gly Arg Pro Asp Gly Arg Gly Thr Pro Ser Ser 1685 1690 Leu Leu Val Ser Thr Ala Pro His His Arg Arg Ser Leu Gly Val Tyr 1705 1710 1700 Leu Gln Glu Gly Pro Val Gly Ser Thr Leu Ser Leu Ser Leu Asp Ser 1715 1720 1725 Asp Gln Ser Ser Gly Ser Thr Thr Ser Gly Ser Arg Gln Ala Ala Arg 1735 1740 Arg Ser Thr Ser Thr Leu Tyr Ser Gln Phe Gln Thr Ala Glu Ser Glu 1745 1750 1755 Asn Arg Ser Tyr Glu Gly Thr Leu Tyr Lys Lys Gly Ala Phe Met Lys 1765 1770 1775 Pro Trp Lys Ala Arg Trp Phe Val Leu Asp Lys Thr Lys His Gln Leu 1780 1785 1790 Arg Tyr Tyr Asp His Arg Val Asp Thr Glu Cys Lys Gly Val Ile Asp 1800 1805 Leu Ala Glu Val Glu Ala Val Ala Pro Gly Thr Pro Thr Met Gly Ala 1810 1815 1820 Pro Lys Thr Val Asp Glu Lys Ala Phe Phe Asp Val Lys Thr Thr Arg 1830 1835 Arg Val Tyr Asn Phe Cys Ala Gln Asp Val Pro Ser Ala Gln Gln Trp 1845 1850 Val Asp Arg Ile Gln Ser Cys Leu Ser Asp Ala

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<213> Homo sapiens

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Pro Asn Val Leu Arg Asn Asp Tyr Leu Asn Arg His Leu Gly Met Val
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                               105
Ala Gln Asp Pro Gln Gly Cys Leu Gln Leu Cys Leu Ser Glu Val Ala
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Asn Gly Leu Arg Asn Pro Val Ser Met Val His Ala Gly Asp Gly Thr
                       135
                                          140
His Arg Phe Phe Val Ala Glu Gln Val Gly Val Val Trp Val Tyr Leu
                 150
                                      155
Pro Asp Gly Ser Arg Leu Glu Gln Pro Phe Leu Asp Leu Lys Asn Ile
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                                  170
Val Leu Thr Thr Pro Trp Ile Gly Asp Glu Arg Gly Phe Leu Gly Leu
                              185
Ala Phe His Pro Lys Phe Arg His Asn Arg Lys Phe Tyr Ile Tyr Tyr
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                                        205
Ser Cys Leu Asp Lys Lys Lys Val Glu Lys Ile Arg Ile Ser Glu Met
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                                          220
Lys Val Ser Arg Ala Asp Pro Asn Lys Ala Asp Leu Lys Ser Glu Arg
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                         235
Val Ile Leu Glu Ile Glu Glu Pro Ala Ser Asn His Asn Gly Gly Gln
                245
                                  250
Leu Leu Phe Gly Leu Asp Gly Tyr Met Tyr Ile Phe Thr Gly Asp Gly
                               265
Gly Gln Ala Gly Asp Pro Phe Gly Leu Phe Gly Asn Ala Gln Asn Lys
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Ser Ser Leu Leu Gly Lys Val Leu Arg Ile Asp Val Asn Arg Ala Gly
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                                          300
Ser His Gly Lys Arg Tyr Arg Val Pro Ser Asp Asn Pro Phe Val Ser
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Glu Pro Gly Ala His Pro Ala Ile Tyr Ala Tyr Gly Ile Arg Asn Met
               325
                                  330
Trp Arg Cys Ala Val Asp Arg Gly Asp Pro Ile Thr Arg Gln Gly Arg
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Gly Arg Ile Phe Cys Gly Asp Val Gly Gln Asn Arg Phe Glu Glu Val
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Asp Leu Ile Leu Lys Gly Gly Asn Tyr Gly Trp Arg Ala Lys Glu Gly
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Phe Ala Cys Tyr Asp Lys Lys Leu Cys His Asn Ala Ser Leu Glu Glu
                  390
                                      395
Gln Ala Thr Glu Asp Gly Ser Pro Glu Ser Leu Gly Arg Pro Ala Ser
               405
                                  410
Gly Val Pro Ile Ser Gly Val Val Leu Asp Thr Gly Val Ser Gly Arg
                              425
Gly Glu Ala Pro Pro Pro Ala Ala Phe Thr Lys Gly Asp Asp Glu
                           440
Leu Ala Met Gly Ala Asp Gln Pro Trp Glu Gly Thr Gly Arg Gly Ala
                      455
Ala Gln Ala Lys Ile Leu Leu Pro Phe Leu Val Phe Ser Ile Phe
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375 380 Thr Cys Ser Asn Pro Gln Arg Ala Gln Leu Cys Glu Asp His Cys Val 390 395 Asp Gly Cys Phe Cys Pro Pro Gly Thr Val Leu Asp Asp Ile Thr His 405 410 Ser Gly Cys Leu Pro Leu Gly Gln Cys Pro Cys Thr His Gly Gly Arg 425 Thr Tyr Ser Pro Gly Thr Ser Phe Asn Thr Thr Cys Ser Ser Cys Thr 440 Cys Ser Gly Gly Leu Trp Gln Cys Gln Asp Leu Pro Cys Pro Gly Thr 455 460 Cys Ser Val Gln Gly Gly Ala His Ile Ser Thr Tyr Asp Glu Lys Leu 470 475 Tyr Asp Leu His Gly Asp Cys Ser Tyr Val Leu Ser Lys Lys Cys Ala Asp Ser Ser Phe Thr Val Leu Ala Glu Leu Arg Lys Cys Gly Leu Thr 505 510 Asp Asn Glu Asn Cys Leu Lys Ala Val Thr Leu Ser Leu Asp Gly Gly 520 Asp Thr Ala Ile Arg Val Gln Ala Asp Gly Gly Val Phe Leu Asn Ser 535 Ile Tyr Thr Gln Leu Pro Leu Ser Ala Ala Asn Ile Thr Leu Phe Thr 550 555 Pro Ser Ser Phe Phe Ile Val Val Gln Thr Gly Leu Gly Leu Gln Leu 565 570 Leu Val Gln Leu Val Pro Leu Met Gln Val Phe Val Arg Leu Asp Pro 585 Ala His Gln Gly Gln Met Cys Gly Leu Cys Gly Asn Phe Asn Gln Asn 600 Gln Ala Asp Asp Phe Thr Ala Leu Ser Gly Val Val Glu Ala Thr Gly **615** . 620 Ala Ala Phe Ala Asn Thr Trp Lys Ala Gln Ala Ala Cys Ala Asn Ala 630 635 Arg Asn Ser Phe Glu Asp Pro Cys Ser Leu Ser Val Glu Asn Glu Asn 645 Tyr Ala Arg His Trp Cys Ser Arg Leu Thr Asp Pro Asn Ser Ala Phe 665 Ser Arg Cys His Ser Ile Ile Asn Pro Lys Pro Phe His Ser Asn Cys Met Phe Asp Thr Cys Asn Cys Glu Arg Ser Glu Asp Cys Leu Cys Ala Ala Leu Ser Ser Tyr Val His Ala Cys Ala Ala Lys Gly Val Gln Leu 710 715 Ser Asp Trp Arg Asp Gly Val Cys Thr Lys Tyr Met Gln Asn Cys Pro 730 Lys Ser Gln Arg Tyr Ala Tyr Val Val Asp Ala Cys Gln Pro Thr Cys 745 Arg Gly Leu Ser Glu Ala Asp Val Thr Cys Ser Val Ser Phe Val Pro 760 Val Asp Gly Cys Thr Cys Pro Ala Gly Thr Phe Leu Asn Asp Ala Gly 775 780 Ala Cys Val Pro Ala Gln Lys Cys Pro Cys Tyr Ala His Gly Thr Val 790 Leu Ala Pro Gly Glu Val Val His Asp Glu Gly Ala Val Cys Ser Cys 805 810 Thr Gly Gly Lys Leu Ser Cys Leu Gly Ala Ser Leu Gln Lys Ser Thr 820 825 Gly Cys Ala Ala Pro Met Val Tyr Leu Asp Cys Ser Asn Ser Ser Ala 840 Gly Thr Pro Gly Ala Glu Cys Leu Arg Ser Cys His Thr Leu Asp Val 855

Gly Cys Phe Ser Thr His Cys Val Ser Gly Cys Val Cys Pro Pro Gly 870 875 Leu Val Ser Asp Gly Ser Gly Gly Cys Ile Ala Glu Glu Asp Cys Pro 885 890 Cys Val His Asn Glu Ala Thr Tyr Lys Pro Gly Glu Thr Ile Arg Val 900 Asp Cys Asn Thr Cys Thr Cys Arg Asn Arg Arg Trp Glu Cys Ser His 920 Arg Leu Cys Leu Gly Thr Cys Val Ala Tyr Gly Asp Gly His Phe Ile 935 940 Thr Phe Asp Gly Asp Arg Tyr Ser Phe Glu Gly Ser Cys Glu Tyr Ile 950 955 Leu Ala Gln Asp Tyr Cys Gly Asp Asn Thr Thr His Gly Thr Phe Arg 965 970 Ile Val Thr Glu Asn Ile Pro Cys Gly Thr Thr Gly Thr Thr Cys Ser 980 985 990 Lys Ala Ile Lys Leu Phe Val Glu Ser Tyr Glu Leu Ile Leu Gln Glu 995 1000 1005 Gly Thr Phe Lys Ala Val Ala Arg Gly Pro Gly Gly Asp Pro Pro Tyr 1015 1020 Lys Ile Arg Tyr Met Gly Ile Phe Leu Val Ile Glu Thr His Gly Met 1025 1030 1035 Ala Val Ser Trp Asp Arg Lys Thr Ser Val Phe Ile Arg Leu His Gln 1045 1050 Asp Tyr Lys Gly Arg Val Cys Gly Leu Cys Gly Asn Phe Asp Asn 1060 1065 Ala Ile Asn Asp Phe Ala Thr Arg Ser Arg Ser Val Val Gly Asp Ala 1075 1080 1085 Leu Glu Phe Gly Asn Ser Trp Lys Leu Ser Pro Ser Cys Pro Asp Ala 1095 1100 Leu Ala Pro Lys Asp Pro Cys Thr Ala Asn Pro Phe Arg Lys Ser Trp 1110 1115 Ala Gln Lys Gln Cys Ser Ile Leu His Gly Pro Thr Phe Ala Ala Cys 1125 1130 Arg Ser Gln Val Asp Ser Thr Lys Tyr Tyr Glu Ala Cys Val Asn Asp 1140 1145 1150 Ala Cys Ala Cys Asp Ser Gly Gly Asp Cys Glu Cys Phe Cys Thr Ala 1160 1165 Val Ala Ala Tyr Ala Gln Ala Cys His Asp Ala Gly Leu Cys Val Ser 1170 1175 1180 Trp Arg Thr Pro Asp Thr Cys Pro Leu Phe Cys Asp Phe Tyr Asn Pro 1190 1195 His Gly Gly Cys Glu Trp His Tyr Gln Pro Cys Gly Ala Pro Cys Leu 1205 1210 1215 Lys Thr Cys Arg Asn Pro Ser Gly His Cys Leu Val Asp Leu Pro Gly 1220 1225 Leu Glu Gly Cys Tyr Pro Lys Cys Pro Pro Ser Gln Pro Phe Asn 1235 1240 1245 Glu Asp Gln Met Lys Cys Val Ala Gln Cys Gly Cys Tyr Asp Lys Asp 1255 1260 Gly Asn Tyr Tyr Asp Val Gly Ala Arg Val Pro Thr Ala Glu Asn Cys 1270 1275 Gln Ser Cys Asn Cys Thr Pro Ser Gly Ile Gln Cys Ala His Ser Leu 1285 1290 1295 Glu Ala Cys Thr Cys Thr Tyr Glu Asp Arg Thr Tyr Ser Tyr Gln Asp 1300 1305 1310 Val Ile Tyr Asn Thr Thr Asp Gly Leu Gly Ala Cys Leu Ile Ala Ile 1315 1320 Cys Gly Ser Asn Gly Thr Ile Ile Arg Lys Ala Val Ala Cys Pro Gly 1335 1340 Thr Pro Ala Thr Thr Pro Phe Thr Phe Thr Thr Ala Trp Val Pro His

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Ser Leu Thr Val Gln Asn Thr Glu Thr Ser Ile Phe Val Ser Met Thr Ser Ala Thr Thr Pro Ser Gly Arg Pro Thr Phe Thr Ser Thr Val Asn Thr Pro Thr Arg Ser Leu Leu Thr Ser Phe Pro Thr Thr His Leu Phe Ser Ser Ser Met Ser Glu Ser Ser Ala Gly Thr Thr His Thr Glu Ser Ile Ser Ser Pro Pro Ala Thr Thr Ser Thr Leu His Thr Thr Ala Glu Ser Thr Pro Ser Cys Thr Thr Thr Thr Ser Phe Ile Thr Ser Thr Thr Met Glu Pro Leu Ser Thr Ile Val Ala Thr Thr Gly Thr Val Lys Thr Thr Val Thr Ser Ser Thr Ala Thr Phe Arg Glu Thr Thr Thr Leu Thr Ser Thr Thr Asp Ile Ser Thr Glu Ser Leu Met Thr Ala Met Thr Ser Thr Thr Arg Leu Thr Ser Ala Ile Thr Ser Lys Thr Thr Leu Thr Ser Leu Lys Thr Thr Ala Ser Arg Pro Thr Ala Asn Ser Thr Leu Ser Ser Leu Thr Ser Ser Ile Leu Ser Ser Thr Leu Val Pro Ser Thr Asp Met Ile Thr Ser His Thr Thr Asn Leu Thr Arg Ser Ser Pro Leu Leu Ala Thr Leu Pro Thr Thr Ile Thr Arg Ser Thr Pro Thr Ser Glu Thr Thr Tyr Pro Thr Ser Pro Thr Ser Thr Val Lys Gly Ser Thr Thr Ser Ile . 615 Arg Tyr Ser Thr Ser Met Thr Gly Thr Leu Ser Met Glu Thr Ser Leu Pro Pro Thr Ser Ser Leu Pro Thr Thr Glu Thr Ala Thr Met Thr Pro Thr Thr Leu Ile Thr Thr Pro Asn Thr Thr Ser His Ser Thr Pro Ser Phe Thr Ser Ser Thr Ile Tyr Ser Thr Val Ser Thr Ser . Thr Thr Ala Ile Thr Ser His Phe Thr Thr Ser Glu Thr Ala Val Thr Pro Thr Pro Val Thr Pro Ser Ser Leu Ser Thr Asp Ile Pro Thr Thr Ser Leu Arg Thr Leu Thr Pro Ser Ser Val Gly Thr Ser Thr Ser Leu Thr Thr Thr Asp Phe Pro Ser Ile Pro Thr Asp Ile Ser Thr Leu Pro Thr Arg Thr His Ile Ile Ser Ser Ser Pro Ser Ile Gln Ser Thr Glu Thr Ser Ser Leu Val Gly Thr Thr Ser Pro Thr Met Ser Thr Val Arg Met Thr Leu Arg Ile Thr Glu Asn Thr Pro Ile Ser Ser Phe Ser Thr Ser Ile Val Val Ile Pro Glu Thr Pro Thr Gln Thr Pro Pro Val Leu Thr Ser Ala Thr Gly Thr Gln Thr Ser Pro Ala Pro Thr Thr Val Thr Phe Gly Ser Thr Asp Ser Ser Thr Ser Thr Leu His Thr Leu Thr Pro Ser Thr Ala Leu Ser Thr Ile Val Ser Thr Ser Gln Val Pro Ile Pro Ser Thr His Ser Ser Thr Leu Gln Thr Thr Pro Ser Thr Pro Ser

														-	C 17 C
865					870					875					880
Leu	Gln	Thr	Ser	Leu 885	Thr	Ser	Thr	Ser	Glu 890	Phe	Thr	Thr	Glu	Ser 895	
Thr	Arg	Gly	Ser		Ser	Thr	Asn	Ala 905	Ile	Leu	Thr	Ser	Phe	Ser	Thr
Ile	Ile				Thr	Pro		Ile		Met	Ser		910 Ser	Pro	Ser
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Ser	930 Ser	Pro	Tyr	Ile	Phe	935 Ser	Thr	Glu	Asn	Val	940 Glv	Ser	Ala	Ser	Tle
945					950					955					960
				965					970				Thr	975	
Thr	Ser	Ser	Ser 980	Leu	Thr	Thr	Ala	Leu 985	Thr	Glu	Ile	Thr	Pro 990	Phe	Ser
Tyr	Ile	Ser 995	Leu	Pro	Ser		Thr 1000		Cys	Pro			Ile	Thr	Ile
Thr	Ile		Pro	Ala		Pro		Asp	Pro		Val	1005 Glu	Met	Asp	Pro
	1010	c1	~ ד ת	ml		1015	D		1		1020				_
1025	1111	GIU	Ala		Ser 1030	Pro	PIO	Thr		Pro 1035	Leu	Thr	Val		
	Thr	Thr	Glu			Thr	Cvs	Pro	Thr	Ser	Tle	Ser	Ile	Gln L	L040 Thr
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Thr	Leu	Thr	Thr	Tyr	Met	Asp	Thr			Met	Met	Pro	Glu	Ser	Glu
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	=	1075					1080				_ :	1085	Gly		
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Trp	Leu	Ser	Asn	Ser	Ser	Val	Ile	Pro	Leu			Pro	Gly	Val	Ser
1105					1110				1	115			_	1	120
			1	L125				3	1130				Thr 1	135	
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Ser		Thr 1155	Pro	Val	Ala				Thr	Pro		Thr 165	Leu	Thr	Ser
Arq			Thr	Ara	Ile			Gln	Met	Thr			Ser	ጥኮሎ	T.011
1	L170				1	L175				1	.180				
1185	Tnr	Thr	Ата			Cys	Asp	Asn			Thr	Trp	Glu		
	Cvs	Δla	Cve		.190 Pro	GT ₁₄	Dhe	80~		195	7	G	Gln	1	200
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		1	.220				1	.225				1	Cys .230		
Pro		Thr .235	Phe	Tyr	Gly		Ser 1240	Сув	Glu	Phe		Val .245	Glu	Gln	Val
	Leu 1250	Asp	Ala	Glu		Phe 255	Cys	Arg	His				His	Leu	Gln
		Gly	qaA		Val		Glu	Glu		Gln		Arg	Gly	_	
	Glv.	Pro	Δla		270	aΓα	T.011	Gln		275 Pro	ת ת	<i>c</i> 1	Glu		280
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<213> Homo sapiens

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(19) World Intellectual Property Organization International Bureau





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WO 02/044340 A3

(54) Title: NOVEL NUCLEIC ACIDS AND POLYPEPTIDES

(57) Abstract: The present invention provides novel nucleic acids, polypeptide sequences encoded by these nucleic acids and uses thereof.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US01/47004

A. CLA	SCIEICATION OF CUDIFCT MATTER						
According to International Patent Classification (IPC) or to both national classification and IPC							
B. FIELDS SEARCHED							
Minimum documentation searched (classification system followed by classification symbols)							
U.S. : 5	U.S.: 536/23.1, 24.3; 435/6						
Documentati	Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched						
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Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)							
GenCore Ve	rsion 5. 1. 3, WEST 2.0		•	•			
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	UMENTS CONSIDERED TO BE RELEVANT						
Category *	Citation of document, with indication, where a	ppropriate,	of the relevant passages	Relevant to claim No.			
X	WO 00/70050 A1 (GENENTECH, INC.) 23 Novem	nber 2000 ((23.11.2000) see entire	1-9			
	patent, especially pages 9, 52-57, Figure 1.		(2212000) 200 00	1-2			
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Further	documents are listed in the continuation of Box C.		See patent family annex.				
- S	pecial categories of cited documents:	-T-	later document published after the inter	mational filing date or priority			
"A" document	defining the general state of the art which is not considered to be		date and not in conflict with the application principle or theory underlying the inve	ntion			
of particu	lar relevance	***	· · ·				
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	which may throw doubts on priority claim(s) or which is cited to						
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"O" document	referring to an oral disclosure, use, exhibition or other means		being obvious to a person skilled in the	art companion			
"P" document	published prior to the international filing date but later than the	*&"		i			
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BNSDOCID: <WO____0244340A3_{_>

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US01/47004

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)					
This	internat	ional report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:			
1.		Claim Nos.: because they relate to subject matter not required to be searched by this Authority, namely:			
2.		Claim Nos.: because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:			
3.		Claim Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).			
Box	II O	servations where unity of invention is lacking (Continuation of Item 2 of first sheet)			
This Plea	Internat se See C	ional Searching Authority found multiple inventions in this international application, as follows: ontinuation Sheet			
1. 2. 3.		As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee. As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:			
4.	ark on l	No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: 1-9, 22-26, SEQ ID NO: 1 Protest The additional search fees were accompanied by the applicant's protest. No protest accompanied the payment of additional search fees.			

Form PCT/ISA/210 (continuation of first sheet(1)) (July 1998)

PCT/U	S01/47004
INTERNATIONAL SEARCH REPORT	

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

The inventions listed as Groups 1-377 do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: The broadest recitation of the claimed product, namely a complementary sequence thereof of SEQ ID NO: 1 of claim 1 is know in the prior art. Hence, the "special" technical feature is not special and is not contribution over the prior art. For example, Baker et al. teach a complementary sequence thereof of SEQ ID NO:1 (WO 00/70059, publication date 23 November 2000, see SEQ ID NO: 1 and Figure 1). The sequence of Baker et al. meets the limitations of the claimed invention. Additionally, the sequences of SEQ ID NOS: 1-93 lack the same technical feature in that SEQ ID NO: 1 is not required or necessary for SEQ ID NO: 2 and visa versa. Similar reasons can be set forth for SEQ ID NOS: 3-93. Likewise the different sequences are both structurally and functionally distinct one from the other. Still further the polynucleotide composed of nucleotides, the polypeptide composed of amino acids, the composition composed of protein and carrier and the antibody composed of peptides are structurally and functionally distinct from each other. Still further, the different methods are distinct in that they require different starting materials, require different reagents and different methodologies that results in differents. This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be search, the appropriate additional search fees must be paid.

Groups 1-93, claim(s) 1-9, 22-26, in part, drawn to an isolated polynucleotide, vector and host cell selected from the group consisting of SEQ ID NOS: 1-93 and complementary sequences thereof, respectively. For example if the Group 1 is elected, the claims 1-9, 22-26 will be examined to the extent that they apply to SEQ ID NO: 1 whereas if the group 93 is elected, the claims 1-9, 22-26 will be examined to the extent that they apply to SEQ ID NO: 93.

Groups 94-186, claim(s) 10, 20, 21, in part, drawn to an isolated polypeptide encoded by any of the polynucleotide comprising the nucleic acid sequence selected from the group consisting of SEQ ID NO: 1-93, repectively. For example, if the group 94 is elected, the claims 10, 20, 21 will be examined to the extent that they apply to the polypeptide encoded by the polynucleotide of SEQ ID NO: 1 whereas of the group 186 is elected, the claims 10, 20 and 21 will be examined to the extent that they apply to the polypeptide encoded by the polynucleotide of SEQ ID NO: 93.

Groups 187-279, claim(s) 11, in part, drawn to a composition comprising the polypeptide encoded by any of the polynucleotide comprising the nucleic acid sequence selected from the group consisting of SEQ ID NO: 1-93, repectively. For example, if the group 187 is elected, the claims 11 will be examined to the extent that it applies to polypeptide encoded by the polynucleotide of SEQ ID NO: 1 whereas of the group 279 is elected, the claims 11 will be examined to the extent that it applies to the polypeptide encoded by the polynucleotide of SEQ ID NO: 93.

Group 280, claim(s) 12, drawn to an antibody.

Group 281, claim(s) 13-15, drawn to a method of detecting a polynucleotide.

Group 282, claim(s) 16, drawn to a method of detecting a polypeptide.

Group 283, claim(s) 17-18, drawn to a method of identifying a compound.

Group 284-376, claim(s) 19, in part, drawn to a method of producing a polypeptide comprising culturing a polynucleotide sequence selected from SEQ ID NO: 1-93 or complementary sequences thereof, repectively. For example if the group 284 is elected, the claim 19 will be examined to the extent that it applies to the polynucleotide sequence of SEQ ID NO: 1 whereas if the group 376 is elected, the claim 19 will be examined to the extent that it applies to the polynucleotide sequence of SEQ ID NO: 93..

Group 377, claim(s) 27-28, drawn to a method of treating.

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